Cross plane transfer of vestibular adaptation to human centrifugation

by

Ian Garrick-Bethell

B.A. Physics
Wesleyan University, 2002

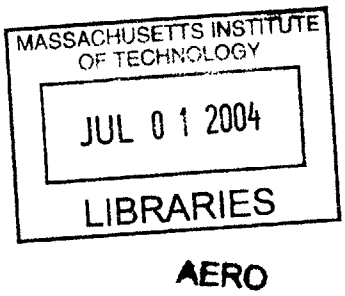
SUBMITTED TO THE DEPARTMENT OF AERONAUTICS AND ASTRONAUTICS
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE IN AERONAUTICS AND ASTRONAUTICS

AT THE

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

JUNE 2004



Signature of Author: _____
Department of Aeronautics and Astronautics
May 14, 2004

Certified by: _____
/Laurence R. Young
Apollo Program Professor of Astronautics
Thesis Supervisor

Accepted by: _____
Edward M. Greitzer
H.N. Slater Professor of Aeronautics and Astronautics
Chair, Committee on Graduate Students

Cross plane transfer of vestibular adaptation to human centrifugation

by
Ian Garrick-Bethell

Submitted to the Department of Aeronautics and Astronautics on May 14 2004, in Partial Fulfillment of the Requirements for the Degree of Master of Science in Aeronautics and Astronautics

Abstract

Human short-radius centrifugation (SRC) is being investigated as a volume-efficient means of delivering intermittent doses of "artificial gravity" to counter the deleterious effects of long exposures to weightlessness. Rotation rates on short radius centrifuges are high to provide the needed g-loading, and therefore entail a variety of unusual vestibular stimuli when certain head movements are made. Since these movements can elicit inappropriate nystagmus, illusions of tumbling, and motion sickness, efforts have been made to adapt people to the stimuli. So far these efforts have been successful in showing that people will adapt to at least one plane of head motion, the yaw (transverse) plane, during supine head-on-axis rotation. However, astronauts must be adapted to all planes of head motion if they are to function normally on the centrifuge. If adaptation to yaw head turns transferred to some extent to pitch (sagittal) plane turns, or any other plane of motion, it would greatly simplify and hasten the adaptation process.

To investigate if transfer of adaptation across planes is possible, 10 subjects in the Experimental Group performed a sufficient number of yaw plane head turns to demonstrate adaptation. Adaptation was indicated by decreases in metrics of the off-axis vestibuloocular reflex induced by the head turns, and by subjective ratings of illusory motion. A block of pitch movements was performed before and after the yaw movements, and these two pitch blocks were compared to assess how much adaptation to pitch head turns had taken place. The same procedure was followed on a subsequent day. A Control Group of 10 subjects performed only the blocks of pitch turns, and their adaptation was compared to the adaptation to pitch turns measured in the Experimental Group.

While both Control and Experimental Groups showed statistically significant signs of adaptation to pitch head turns, we failed to find any significant differences between the amounts of adaptation. If true, this result implies that adaptation to SRC may need to be performed one plane of motion at a time. Additionally, it implies that the brain and vestibular system does not build up a generalized model of SRC stimulation, but rather builds adaptation one input at a time.

Thesis supervisor: Laurence R. Young
Title: Apollo Program Professor of Aeronautics and Astronautics

This work was supported by the National Space Biomedical Research Institute through a cooperative agreement with the National Aeronautics and Space Administration (NCC 9-58).

Acknowledgments

I am most grateful to Laurence Young for giving me the opportunity to work in this lab and conduct research that may one day help send humans off into deep space. I am also happy to have had gained some proposal writing experience while onboard.

I must thank Alan Natapoff for providing many invaluable hours of instruction on how to analyze and think about my data. I am also most grateful for the lunches and Arizona green tea.

I thank Thomas Jarchow for his generous support in all matters scientific and technical.

I thank Heiko Hecht for showing me the ropes during the first few months I was here and helping me establish my pilot studies.

I thank the undergraduates who helped with my experiment: Ben Feinberg, Ethan Post, Gita Srivastava, Amy Wu, and Cemocan Yesil.

I thank Jessica Edmonds and Sophie Adenot for being such delightful officemates.

I thank Erika Wagner for helping me with the occasional question and for being such a delightful ex-officemate.

I thank Chris Carr for taking some of the photos in this thesis.

I thank my subjects for all of their wonderful little eye movements, but I'm not allowed to name them.

I am also indebted to Liz Zotos for all of her administrative assistance.

And of course, I owe very much to my Mom, Dad, and Howard. Thank you for all of the support.

This work was supported by the National Space Biomedical Research Institute through a cooperative agreement with the National Aeronautics and Space Administration (NCC 9-58).

Table of Contents

List of figures and tables

Chapter 4 - Data Analysis figures

Chapter 5 – Results figures

Tables

"Let us take graceful attitudes!"

From Jules Verne's *Autour de la Lune*, 1870.
Woodcut by Emile Bayard.

Chapter 1 – Introduction

1.1 The status of space exploration

At the time of this writing President George Bush and NASA have charged the United States with the first comprehensive program to explore another world since the Apollo program. According to the new national vision, robotic missions will begin paving the way to the Moon in 2008, and astronauts should step foot on its soil again by 2020. Whether or not NASA fulfills this refreshing vision remains to be seen. Among the obstacles of obtaining money from Congress, producing sustainable budgets and long term plans, and convincing the public of the venture's worth, is not least the technology required for long duration spaceflight. Many brand new systems such as landing vehicles, command modules, and rovers will have to be built. Talk of building such spaceships may conjure up images of rocket scientists and physicists crunching equations on blackboards, but there is a unique component of manned spaceflight that requires engineers to understand how people are put together, as well as machines. Whenever people return to space beyond low earth orbit, the space environment will provide a variety of damaging health effects that need to be characterized and mitigated. Engineers with knowledge of medicine, physiology, and biology and will have to ensure that the hardware being built will accommodate the frailty of human beings.

Even after the Apollo, Skylab, Mir, and Shuttle programs, a large quantity of biological research still needs to be done before we can defeat all of the dangers of long-duration spaceflight. NASA's planned use of the International Space Station primarily to solve the physiological challenges facing humans is evidence of this fact. Humans have little experience traveling to, living, and working on worlds beyond Earth. Indeed, since the beginning of human space exploration only 24 people have ventured beyond Earth's radiation belts. Of those 24, all of whom were American Apollo astronauts, only 12 actually walked on the Moon. Of those fortunate 12, only the last 2 stayed longer than 72

hours on the surface. And in the last 32 years no one has made the trip back. Many new challenges are sure to present themselves as people realize longer stays on the Moon, Mars, and other bodies throughout the solar system.

1.2 Environmental obstacles

Among the dangers that space explorers face are low-pressure environments, extreme temperature changes, high levels of radiation, micrometeroid impacts, cramped and isolated living quarters, and high accelerations. Also affecting explorers is the weightlessness that comes from the unusual nature of being in orbit around a planet or star. The damaging health effects of weightlessness are subtler than most other biological effects, but can be equally deleterious for long missions. Effects such as bone loss, muscle wasting, and reduced cardiovascular output due to reduced loading can put an explorer at great risk when they start operating at their destination or back on Earth. The effects of neurovestibular readaptation and motion sickness in weightlessness are both a nuisance and can affect performance during the flight. Some of the adverse effects of weightlessness may well carry over to living in low-g environments such as the Moon and Mars (Larson and Pranke, 1999). In order to combat these risks, engineers have been tasked with developing biological countermeasures.

Most protections from the space environment focus on removing the threat, but this has not been true for weightlessness. For example, the threat from radiation is reduced by using orbits with minimum exposure and by providing the spacecraft with as much shielding as practical. For weightlessness however, the problem is so fundamental to the orbital motion of space travel, efforts to prevent the harmful effects are have so far been merely curative. Extensive exercise regiments have been employed with the goal of increasing loading on bones and muscles, but they do not offer complete protection. The alternative countermeasure approach to weightlessness would be to provide the missing gravity stimulus itself, either over long durations of time, or for short exposures. Such artificial gravity (AG) could be administered by creating a rotating environment, or centrifuge, for astronauts.

1.3 The use of centrifuges

The use of centrifuges to provide artificial gravity in space was suggested long before spaceflight was a reality. The first scientist-engineer to seriously consider providing space explorers with artificial gravity was Tsiolkovksy in 1911, who suggested that a rotating structure could provide a convenient on/off gravity environment if it should ever be "proven that people could not live without gravity" (Shipov, 1991). Following up on Tsiolkovsky's ideas in 1918, Capt. Potocnik of the Austrian Imperial Army, writing under the pseudonym of Hermann Noordung, published the first detailed space station designs (Von Braun, 1966). Noordung proposed a rotating wheel-shaped vehicle to provide the users with AG at the rim. Space visionaries Wernher von Braun and Willy Ley would later publicize these ideas in the United States during the 1950s in an effort that greatly enhanced public awareness of the possibilities of spaceflight. Von Braun's own vision of a rotating wheel-shaped space station was embodied in Arthur C. Clarke's 1968 sci-fi epic *2001: A Space Odyssey*, and also appeared in Stanley Kubrick's movie screen version of the book, Figure 1.1. Laurence Young (2003) reviews and provides a modern outlook on the advantages and limitations of using AG.

The only actual implementation of what may be considered a large space centrifuge was the rotating tethered connection between the US Gemini XI spacecraft and an Agena docking-target vehicle in 1966 (Hacker, 1977). With a radius of 15 m and a rotation rate of 0.15 rpm (0.6 g), the two spacecraft rotated about their center of gravity for about 3 hours. Small oscillations were experienced after initial spin up, but they quickly died out. The final centripetal acceleration was sufficient enough for the astronauts to observe objects "falling" within the cabin in a direction tangent to the tether, but was small enough that they reported no physiological effects of rotation. This demonstration exercise involved a large radius rotation scheme that would be difficult to implement on a bigger and more complex spacecraft. A substantial amount of propellant would be required to accelerate a large spaceship to rotational speeds capable of providing useful levels of AG, thereby increasing the launch mass of the vehicle. In addition, even more

propellant would need to be burned to decelerate the rotating craft upon reaching its destination.

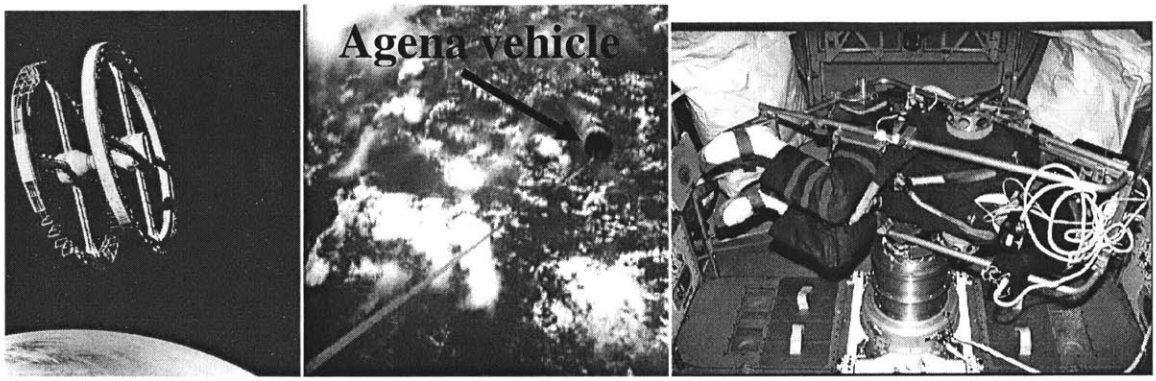


Figure 1.1. Space rotators, conceptual and real, over the last 50 years. Left, Von Braun's 1950s concept of a space station in lunar orbit in the sci-fi movie *2001: A Space Odyssey* (GRIN, 2004), center, a view of the Gemini XI tethered rotation with the Agena vehicle, 1966 (JSC, 2004), and right, the Space Shuttle STS-42 IML centrifuge, 1992 (JSC, 2004). It is clear that space rotators have generally gotten smaller.

Modern AG efforts have focused on using volume efficient short-radius centrifuges (SRC) that rotate inside of a spacecraft (Young, 1999). One such device flew on the STS-42 IML mission, but was used to study vestibular systems, not as a countermeasure, Figure 1.1. When used as a countermeasure, a SRC user might be provided with intermittent doses of gravity that could be combined with exercise, or administered while sleeping, if deemed necessary. The rotation rate of a SRC on the order of 2-3 meters in radius must be high if it is to provide 1-G of gravity, since the centripetal acceleration, or gravity equivalent, it delivers is dependent on the square of the rotation rate ($a_c = r\omega^2$). Several organizations have recently built SRC centrifuges that meet these requirements to test the feasibility of administering intermittent AG (Caiozzo et al., 2004; Iwase et al., 2003). Future studies to demonstrate the efficacy of SRC are planned using subjects exposed to 6 degree tilt head down bed rest (Paloski et al., 2003). At MIT, a 2 m radius centrifuge was constructed by Peter Diamandis (1988), and has made possible a number of studies.

1.4 The side effects of centrifugation

Artificial gravity produced by rotation is not without adverse side effects, for both small and large radius devices. Perhaps the most physically obvious of these effects is that while living in a large-radius rotating environment, moving about radially from the axis of rotation will result in changes in the effective gravity field. Such changes cause objects to weigh different amounts at different radii, and also entail Coriolis pseudo-forces that act tangential to radius. Those who are exposed to AG with a high enough rotation rate will also experience the effects of cross-coupled vestibular stimulation while moving their head in and out of the plane of rotation. As a result, nystagmus ensues that would be the correct response for a rotating visual field, but inappropriately causes retinal slip in a fixed visual field. In addition, one may experience illusory sensations of tumbling and motion sickness. Characterizing these vestibular effects and understanding how astronauts can adapt to them is important if astronauts using AG are to eventually make completely unrestrained head movements free from adverse side effects.

1.5 Motivation for this study

Some experiments have shown that adaptation to the vestibular effects of head movements during centrifugation is possible. Studies performed on the ground with the MIT 2 m SRC have demonstrated tolerance and adaptation to yaw-plane (transverse) head motions performed during supine 23 rpm (1-G at the feet) clockwise rotation (Hecht et al., 2002; Young et al., 2001). Adaptation protocols performed in the light have yielded reductions in motion sickness scores, illusory sensations of tumbling, VOR time constants, and slow phase eye velocity (SPV) amplitudes. While this adaptation makes SRC a promising tool, it has only been demonstrated for yaw head movements. Astronauts, however, need to adapt to motion in all planes if they are to function normally while rotating. If some of the adaptation gained from movements in the yaw plane could transfer over to movements made in the pitch plane (midsagittal), or any other plane, it would reduce hasten the process of adaptation in that plane, Figure 1.2. Astronaut adaptation training would be simpler, since each plane of motion would not

have to be adapted separately. Additionally, any such transfer should yield insight into how the brain processes different vestibular stimuli.

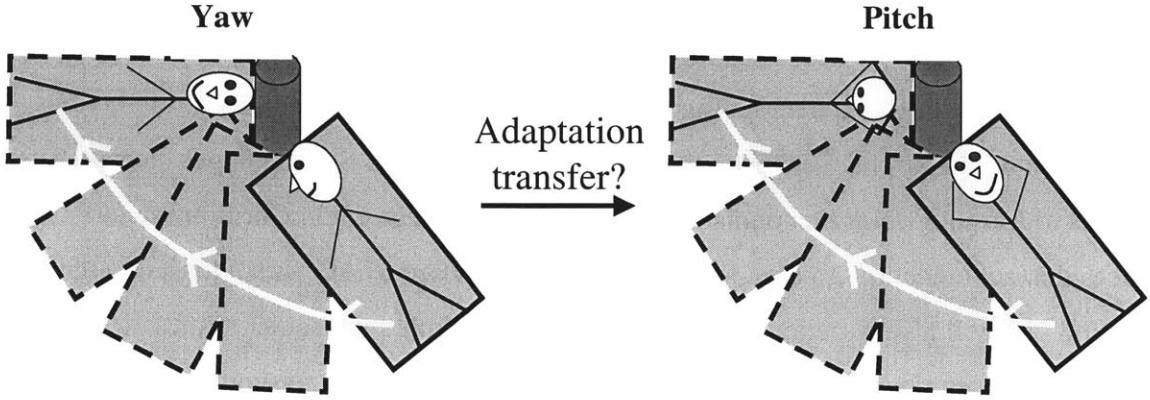


Figure 1.2 Will adaptation to yaw movements transfer to pitch movements while rotating?

1.6 Hypothesis

Subjects who are exposed to an adaptation series of yaw head movements will simultaneously build up some generalized adaptation to pitch movements. The adaptation to yaw will be judged by reductions in motion sickness scores, illusory sensations of tumbling, the time constant of the vestibuloocular reflex, and slow phase eye velocity peak amplitude. Pitch movements performed before and after the yaw movements will be assessed for the same signs of adaptation (the Experimental Group), and a comparison will be made with a Control Group that performs no yaw movements.

Objectives:

1. Understand the pitch adaptation process and determine if for any reason, however unlikely, pitch head movements do not adapt to 23 rpm supine head-on-axis rotation.

2. Determine if the pitch adaptation process is altered in any way, for better or worse, by the performance of a series of yaw movements.

3. Make recommendations for future work on developing efficient adaptation protocols for all head motion planes.

1.7 - Thesis organization

Chapter 1 – Introduction. This introductory section.

Chapter 2 – Background. Provides a background on the adverse effects of weightlessness, and how centrifugation aims to alleviate those problems. With a focus on recent work, discusses the vestibular system, aspects of vestibular adaptation, the physiology of adaptation, and adaptation to rotational environments. Past research is also presented that addresses transfer of adaptation gained from one environment or stimulus to another environment or stimulus.

Chapter 3 – Methods. Explains in detail the experiment protocol and the data collected.

Chapter 4 – Analysis. Provides an explanation of how the data was analyzed, and summarizes significant results. A new data editor for eliminating noise in eye movement records is introduced

Chapter 5 – Results. Presents all of the data from the Control and Experimental Groups.

Chapter 5 – Discussion. Explores the results of Chapter 4 and establishes that yaw adaptation did occur. Compares the pitch movement data in the Control and Experimental Group and draws conclusions about why or why not transfer may have occurred.

Chapter 6 – Conclusion. Summarizes the results and makes recommendations for future work on adaptation to short-radius centrifugation.

Chapter 2 - Background

2.1 Adverse effects of spaceflight

2.1.1 The spaceflight environment

As stated in the Introduction, spaceflight poses numerous health risks to humans. The most ubiquitous danger is probably the constant need for separation from the vacuum of space. Rapid exposure of a crew to vacuum would be a very serious event, and not a scenario they would be expected to face with any regularity. However, astronauts are forced to confront the vacuum outside in other ways by living in the reduced pressure environments of spacesuits and space vehicles. Vehicles may be operated at a lower pressure to limit structural loading, and they can put astronauts at risk for decompression sickness and air embolisms (Parker and West, 1973). Spacesuits must also be designed so that segments are stiff enough to accommodate the air pressure inside, but maneuverable enough to avoid fatiguing the astronaut.

A more subtle threat in space is the rain of high-energy particles that stream from the solar wind and other galactic sources. Astronauts can be shielded from some of these particles, but solar flares can lead to dangerously high fluxes. High-energy heavy ions from galactic space pose an unavoidable risk because added shielding will merely increase the chance of these particles creating a larger stream of secondary particles. The ultimate health effect of these particles in the short term could be acute radiation syndrome, or cancer in the long term (Ohnishi, 2002).

Still other problems include space motion sickness (Berry, 1970), psychological isolation (Kanas et al., 2002), and reduced immune function (Sonnenfeld and Shearer, 2002). In the next three sections, the problems of cardiovascular deconditioning, bone loss, and muscle loss are briefly reviewed, since these three areas stand to benefit the most from SRC. These are also the areas where the health effects are most visible.

2.1.2 Muscle loss

In a microgravity environment muscles do not need to overcome the usual loading that they experience on Earth. The effect of the reduced loads is believed to be primarily a decrease in protein synthesis in muscles (Fitts et al., 2000). As a result, muscle atrophy and a loss of force and power occurs, especially in "antigravity muscles" that normally work constantly against gravity to maintain posture and provide locomotion. Recent studies to quantify the amount of muscle loss have used MRI before and after spaceflight. Examination of cosmonauts after 6 months of Mir flight showed 6-20% volume losses in calf plantar flexors, such as the soleus antigravity muscle (Zange et al., 1997). Studies have also shown preference for loss of type II fibers over type I, which are smaller, and a general relationship between fiber size and loss rate has been documented (Edgerton and Roy, 1996). In both metrics of fiber loss and volume loss, a wide range of differences are found, and could be due to different exercise routines and styles. Solving the problem of muscle loss is essential if crews are to be able to successfully perform extravehicular activities.

2.1.3 Bone loss

Anyone who has studied bone growth and destruction will have encountered Wolf's law, which states that bones will modify themselves in response to the mechanical forces that act on them (Wolf, J., The Law of Bone Transformation, 1892). That is, if there are extensive loads on a bone, it will grow, but if the bone mass is higher than it needs to be for its loading, it will be resorbed. In spaceflight the bones that normally bear the postural load obviously experience much reduced forces when astronauts are not exercising, and possibly even when they are. While there are many unknowns about bone loss due to weightlessness and its cellular and biochemical pathways, the major finding has been that depletion of calcium always takes place (Turner, 2000). Calcium uptake in the intestines is reduced, and excretion through in the urine is increased, which may also increase the risk of renal stone formation. Effects of weightlessness on

lowering bone density vary widely according to the bone being measured and the individual, but general findings show increased losses in the pelvis, lumbar vertebrae and femoral neck (Turner, 2000). Whether these processes are a result of increased resorbtion, decreased formation, or some other osteocyte interaction, is unknown (Turner, 2000). Solving the biochemical problems of bone loss remains a major challenge, and would undoubtedly benefit those on Earth suffering from bone diseases such as osteoporosis. Conversely, pharmacological treatments for bone loss in space may be similar to those used for osteoporosis. Either way, bone loss must be solved for long duration spaceflight to avoid fractured or broken bones when returning to a non-weightless environment.

2.1.4 Cardiovascular deconditioning

When first entering orbit, gravity no longer pulls blood towards the feet, and fluids shift towards the upper parts of the body and face. To compensate for the changes in fluid distribution and pressure, large amounts of fluid are excreted. This excretion causes a condition known as hypovolemia, or low blood volume. Hypovolemia is thought to be a major contributor to postflight orthostatic intolerance (Zhang, 2001), which affects some, but not all astronauts after landing. Those affected may experience trouble walking, dizziness, lightheadedness, and fainting, and could possibly experience greater difficulty in helping themselves in an emergency or novel situation. Reductions in cardiac muscle mass may be another long term result of microgravity. A few recent studies of astronauts and patients living in 6 degree head down tilt have yielded greater insight into causes of cardiovascular deconditioning. Some of this work, as summarized in Zhang (2001), points to the possibility that redistribution of internal pressures and flows result in localized adaptive changes in arterial smooth muscle and cardiac muscle (Zhang, 2001; Zhang et al., 1996). These changes do not provide sufficient peripheral vascular resistance upon return to Earth gravity (Zhang, 2001). Keeping these peripheral centers in a state of readiness for gravity should be a primary accomplishment of any cardiovascular countermeasure.

2.1.5 Existing countermeasures and their efficacy

The International Space Station (ISS) has several exercise devices that are meant to limit bone, muscle, and cardiovascular deconditioning, Figure 2.1. The devices include a treadmill with a down-pulling harness to simulate Earth weight, a cycling machine, and a resistive exercise unit. In ground based studies the resistive device provided muscle mass increases comparable to a control group that performed free weight exercises, but was not effective in stimulating bone (Schneider et al., 2003). The loss of bone mass during spaceflight has generally shown resistance to countermeasure efforts, possibly because dynamic impact loading is an essential element in the maintenance of bone mass. As for cardiovascular deconditioning, exercise alone on a treadmill or cycle may not be sufficient because it does not provide the peripheral vessels with the normal 1-G fluid distribution. Lower body negative pressure (LBNP), and exercise combined with LBNP has shown mixed results in some ground studies (Zhang, 2001), but again, more studies are needed. Part of the difficulty with LBNP may be that it cannot simulate the local cerebral vascular pressures (Zhang, 2001).

Figure 2.1 Current countermeasure exercise devices on ISS (NASA, 2003). Left, Cycle Ergometer with Vibration Isolation System (CEVIS), center, Interim Resistive Exercise Device (IRED), and right, Treadmill Vibration Isolation System (TVIS).

2.1.6 SRC as a countermeasure

The use of SRC for artificial gravity has the potential to approximately reproduce the gravity on Earth, which could be of great benefit for moderating changes in cardiovascular function, and potentially bone and muscle loss. Studies by Vernikos (1996, 1997) showed that even intermittent exposures of 1-G centrifugation, or 2 hours of standing, may be enough to reduce orthostatic intolerance. Rats exposed to tail suspension also showed resistance to bone and muscle loss when exposed to intermittent 1-G (Fitts, 2000). When combined with exercise, SRC could be even more effective.

Before SRC AG can be implemented in any long duration flight, it must be demonstrated that its benefits are real, and it must be demonstrated that it is tolerable to those who use it. As stated above, demonstration of efficacy has partially been established, and more comprehensive validation plans are underway (Paloski et al., 2003). As for tolerance to SRC, exposure to rotation on the order of 20-30 rpm is quite provocative to the vestibular system, and produces a number of side effects (Section 1.4). In the past it was believed that adaptation to such high speeds would not be possible, but results at MIT have shown otherwise (Young et al., 2001). Nonetheless there are still many remaining questions about vestibular adaptation to SRC, and so a background of the vestibular system is presented below before going any further.

2.2 Vestibular physiology

2.2.1 Introduction

The vestibular system is responsible for providing the brain with information on the body's orientations and accelerations in space. Vestibular sensors in the ear detect motion and transduce it into electrical impulses carried by nerve cells. The brain translates the information it receives into perceptions of rotation, linear motion, and body

tilt. A complete internal estimate of motion is generated, and the body is thus able to maintain balance and track visual targets while moving.

Located in the inner ear in a section of temporal bone called the labyrinth, the vestibular system is comprised of two units for detecting motion. One is the otolith organs for sensing linear motion, and the other is the semicircular canals for sensing rotational motion, Figure 2.2. Within the labyrinth, these sensors are separated from the bone by the perilymph fluid. Rotational and linear accelerations are sensed by the motion of the endolymph fluid inside of the canals and the otolith organs.

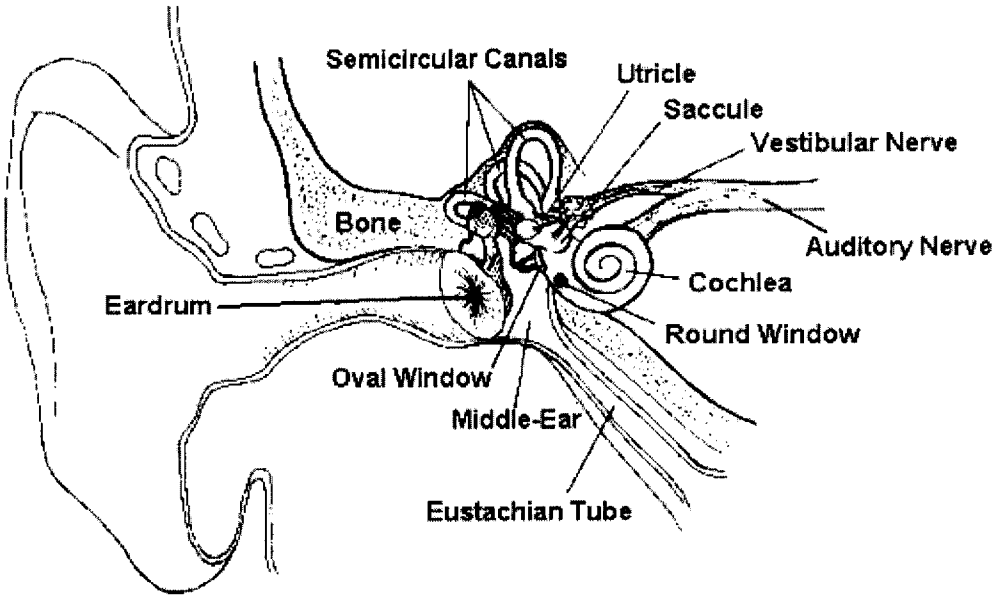


Figure 2.2 Inner ear anatomy (VEDA, 2004)

2.2.2 Otolith physiology

The otolith organs consist of the utricle and the sacule, two membranous sacs that detect head tilt and linear acceleration, Figure 2.3. Within each sac is a portion of membrane that contains a bed of hair cells called the macula. When unperturbed, these hair cells have a constant firing rate of about 100 action potentials per second, and continually innervate the 8th nerve (vestibular nerve). Bundles of cilia extend upward from the

macula hair cells into a gelatinous mass called the otolithic membrane. Suspended within this membrane are small calcium carbonate concretions called the otoconia.

Linear accelerations and head tilts cause the otolithic membrane to slide over the hair cells, bending the cilia forwards or backwards. Depending on the direction that the cilia are bent, the firing rate of the hair cells is modulated up or down from the resting rate. A single long cilia on each cell called the kinocilia establishes the relationship between tilt direction and firing rate: adjacent cilia (stereocilia) that are tilted away from the kinocilia provide a decrease in firing rate and stereocilia that are tilted towards the kinocilia increase the firing rate, Figure 2.4. Innervations of the 8th nerve make their way to the vestibular nucleus, where the brain further processes the signals. Motion can be detected in all axes because the saccule and utricle are in approximately orthogonal orientations, but this does not preclude potential confusion in determining if cilia have been bent from linear motion, or due to head tilt. Once linear acceleration stops, the cilia will return to rest and the sensation of motion (or illusory tilt) will cease.

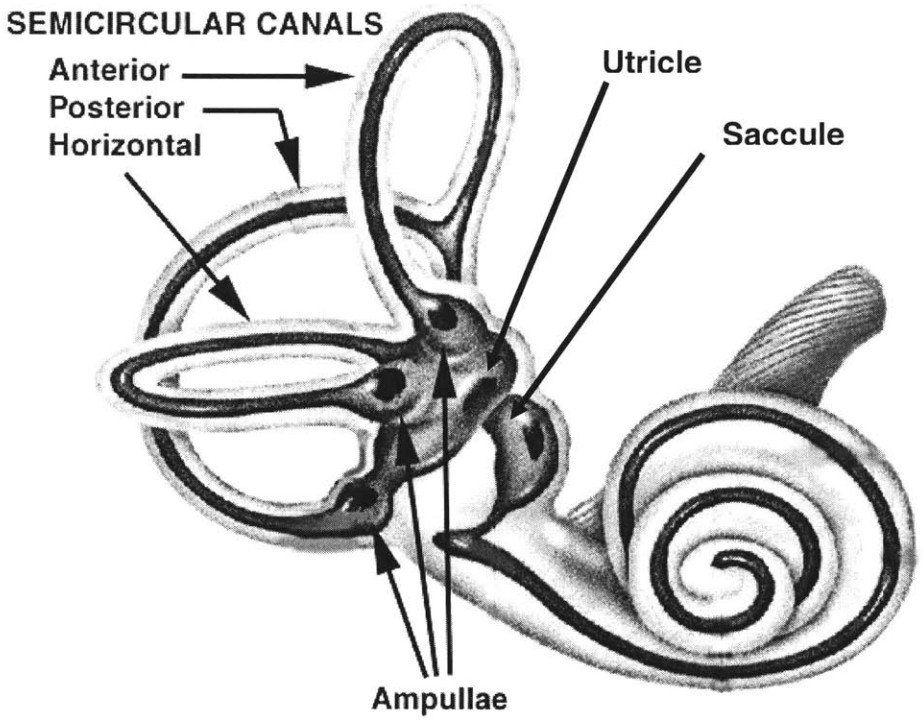


Figure 2.3 Closer view of the semicircular canals and otolith organs (MIT, 2004).

2.2.3 Physiology of the semicircular canals

Three approximately orthogonal fluid filled canals provide information on angular accelerations of the head. At the base of the canals, the bulge at the ampula houses a gelatinous mass referred to as the cupula, Figure 2.5. The cupula extends upwards from its base at the crista and seals against the opposite side of the ampula. Similar to the structural organization found in the otolith organs, hair cells residing in the crista have cilia bundles rising upward that are embedded in the cupula. As the head rotates, the endolymph in the canals lags behind and displaces the cupula. This displacement modulates the firing rate of the hair cells from the resting steady state rate. The 8th nerve is innervated, the signal is processed in the vestibular nucleus, and a sensation of motion results.

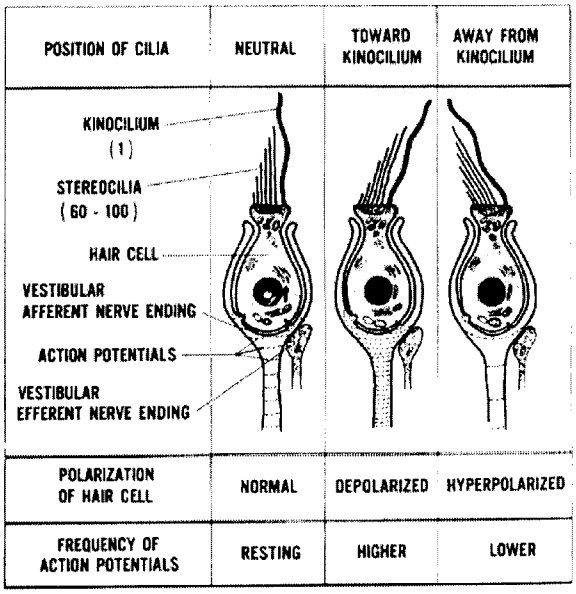


Figure 2.4 Physiology of vestibular hair cells and the relation between firing rate and bend direction (MIT, 2004).

Once the endolymph in the canals catches up with the rotation rate of the head, the cupula relaxes and the sensation of motion eventually ceases. The approximately orthogonality of the three canals permits rotation to be sensed in all directions. While the canals are not perfectly orthogonal, they can each be considered to detect motion in three rotational directions: the horizontal canals sense primarily yaw, the anterior canals sense primarily roll, and the posterior canals detect primarily pitch. In this thesis, the projection of the canal axes onto the body axes will constitute theoretical "pitch canals", "yaw canals", and "roll canals."

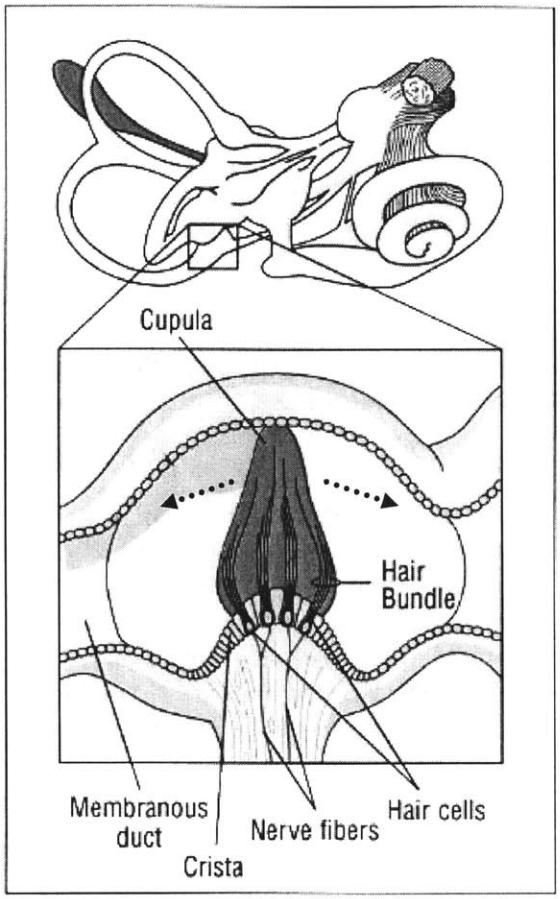


Figure 2.5 Illustration of the cupula and its embedded hair cells (MIT 2004). Arrows indicate possible deflections due to the lag of the endolymph during head rotation.

2.3 The vestibuloocular reflex (VOR)

2.3.1 Eye stabilization

The vestibular system plays a major role in helping stabilize the eyes in response to head movements. If the eyes did not compensate for motion of the head, the eyeball would rotate with the head during movements and cause the image on the retina to slip (retinal slip). This slippage would make it impossible to focus on an object even during simple perturbations such those induced during walking. To compensate, accelerations sensed by the semicircular canals and otolith organs are coupled to the eye muscles through the vestibular nucleus and nodulus of the vestibulocerebellum. When a head turn is made the afferent signals from one set of canals are reduced in frequency, while the other set of

canal afferents is increased in frequency. The vestibular nucleus combines this information and sends efferent signals to the appropriate eye muscles to induce a compensatory velocity step in a direction opposite direction of the head turn. The ratio of eye velocity to head velocity is the gain of this reflex (the vestibuloocular reflex (VOR)), and is typically near 0.7.

2.3.2 VOR and nystagmus

If the rotational acceleration of the head is high enough, the VOR motion may not be able to fully compensate before reaching the maximum angular deviation of the eye. Upon reaching this endpoint, or earlier, the eye will reset back to neutral with a higher velocity, and then move again in the compensatory direction. The rhythmic process continues in what as known as nystagmus, even after the head acceleration has stopped. Eventually, the velocity of the compensatory movements, which is the slow phase velocity (SPV), decays back to zero. The decay of SPV is usually modeled as a decreasing exponential function of the form $Aexp(-t/\tau)$, where A is the maximum SPV and τ is the time constant for the decay. The mechanical properties of the cupula help determine the length of the decay time constant.

2.3.3 VOR time constants

During nystagmus the time constant for the decay is longer than simply the relaxation time constant of the cupula. The decay time of nystagmus beyond the time constant for the cupula can be conceptualized as the brain storing additional rotational velocity information that prolongs the eye movements, known as velocity storage (Raphan et al., 1979; Wilson and Melvill-Jones, 1979). The additional stored velocity effectively adds to the VOR time constant of the cupula, and is called the central time constant. The cupula time constant is referred to as the peripheral time constant, and is typically shorter. Work is still ongoing in trying to isolate the length of the peripheral constant (e.g. Dai et al., 1999).

2.3.4 VOR adaptation and physiology

The central time constant is not fixed by mechanical properties as is the peripheral time constant. After repetitive exposure to a strong stimulus, the overall VOR response will decrease due to a decrement in the central constant, and much research has been done to characterize these changes. As for VOR gain, this too can decrease after repetitions, and the decrease will be especially strong if the stimulus is given in the light. The lighted conditions provide the retinal slip that the VOR movement is attempting to compensate for, and the reflex will appropriately adapt to a lower velocity.

Recent efforts have focused on understanding the physiological elements in the brain that determine the length of the central time constant. The nodulus of the vestibulocerebellum has long been known to be important in vestibular adaptation (Singleton, 1967; Waespe et al., 1985), but research over the past dozen years has focused on elucidating its exact role. Research by Cohen and others shows that nodulectemy abolishes VOR adaptation and returns time constants to pre-adaptive values in monkeys (Cohen et al., 1992). They propose that in the absence of confirming cues, the nodulus and uvula of the vestibulocerebellum sense the inappropriate extension of VOR, and lower it appropriately. Other efforts have shown the role of the uvula in orienting VOR to the direction of the ambient gravito-inertial (GI) acceleration (Cohen et al., 2002; Sheliga et al., 1999). One study has distinguished the role of the nodulus as mainly a source of semicircular canal inputs, while the uvula receives otolith afferents (Maklad and Fritzsch, 2003), but does not preclude the nodulus from integrating GI cues. Additionally, separate parts of the nodulus have been shown to regulate distinct axes of velocity storage. Nodulectomy of the lateral part of the nodulus affected horizontal VOR velocity storage, and nodulectomy of the central part affected roll and torsional VOR in a study of rhesus monkeys by Wearne et al. (1998). Of particular relevance to this study may be work that shows that in rabbits the nodulus "influences remembered head position in space derived from previous optokinetic and vestibular stimulation" (Barmack et al., 2002).

2.3.5 Velocity dumping

There is strong evidence that velocity storage is regulated by otolith cues. The phenomenon of "nystagmus dumping" involves the quenching of VOR by quickly changing the orientation of the head during post-rotational nystagmus. A simple way to induce VOR dumping is to spin a rotating chair while upright, then stop the motion of the chair abruptly, and quickly pitch forward. The origin of this decay was believed to be due to the influence gravity acting as a conflicting cue, signaling that the velocity was being overestimated. When a similar procedure was performed in weightlessness, VOR was not quenched as greatly as it was in ground experiments, which helped confirm the otolith conflict model (Oman and Balkwill, 1993). Recent work on otolith-canal interactions during dumping is still ongoing (e.g. Bockisch et al., 2003). Most studies are consistent with models that show the nodulus, which regulates the central time constant, integrates gravity cues in its model of motion and the most appropriate eye response.

2.4 Motion sickness and its relation to vestibular inputs

2.4.1 Conflict theory

Conflict between the vestibular system, visual inputs, tactile cues, and other perceptual sources is believed to be responsible for the generation of motion sickness (Reason, 1975). A classic example is reading while riding in a car. Focusing on the text provides the reader with a stable visual reference frame, while the otolith organs and semicircular canals conflict with this perception by sensing linear and rotational accelerations due to the motion of the car. The driver will seldom get sick because he is able to observe and anticipate visual changes that are in synchrony with his vestibular inputs.

2.4.2 The VOR time constant and motion sickness

Recent research has pointed to a connection between the reduction of the VOR time constant and a reduced susceptibility to motion sickness. A correlation between motion

sickness susceptibility and the velocity storage mechanism has been observed in parabolic flight (DiZio and Lackner, 1991). Bos found a similar relationship and asserted that generally "the stronger the velocity storage, the sicker the subject" (Bos, Bles, and Graaf, 2002). Based on these findings, recent work has been done to determine if reducing the time constant by drug administration would also have an effect on motion sickness. The drug Baclofen has been shown to reduce the VOR time constant in monkeys (Cohen, Helwig, and Raphan, 1977), and pilot studies with humans have yielded similar results (Young et al., 2003). All of these studies also imply that reduction in the VOR time constant should be a good metric for assessing how susceptible an individual might be to future SRC sessions, and how adapted they have become to SRC in general.

2.5 Vestibular stimulation during centrifugation

2.5.1 Nystagmus and illusory motion

During centrifugation at a constant velocity the semicircular canals will eventually be at equilibrium. However, during certain head motions they will be perturbed and elicit nystagmus that is accompanied by illusory sensations of motion. The nystagmus and illusions are a result of moving canals into and out of the plane of rotation as the head is moved. For example, if during supine head-at-center rotation, which is used in this study (Figure 1.2), the subject turns from nose up (NU) to right ear down (RED) they will move the pitch plane into the plane of rotation, and the roll plane out of the plane of rotation, Figure 2.6. With the pitch plane now being stimulated, the cupula is displaced and the subject experiences nystagmus and illusions of pitch motion. If the direction of centrifugation is CW, then the subject should feel pitch backward motion, which given the new orientation of their head, is correct (Figure 1.2). Meanwhile, the roll canal has been removed from the plane of rotation and is decelerated. The resultant deflection of the cupula should produce torsional VOR and illusions of roll in the CCW direction, although the dominant illusion has been found to be in the pitch direction. Such head

motions often produce motion sickness because the illusory sensations conflict with the visual, tactile, otolith, and expected vestibular cues that the subject experiences.

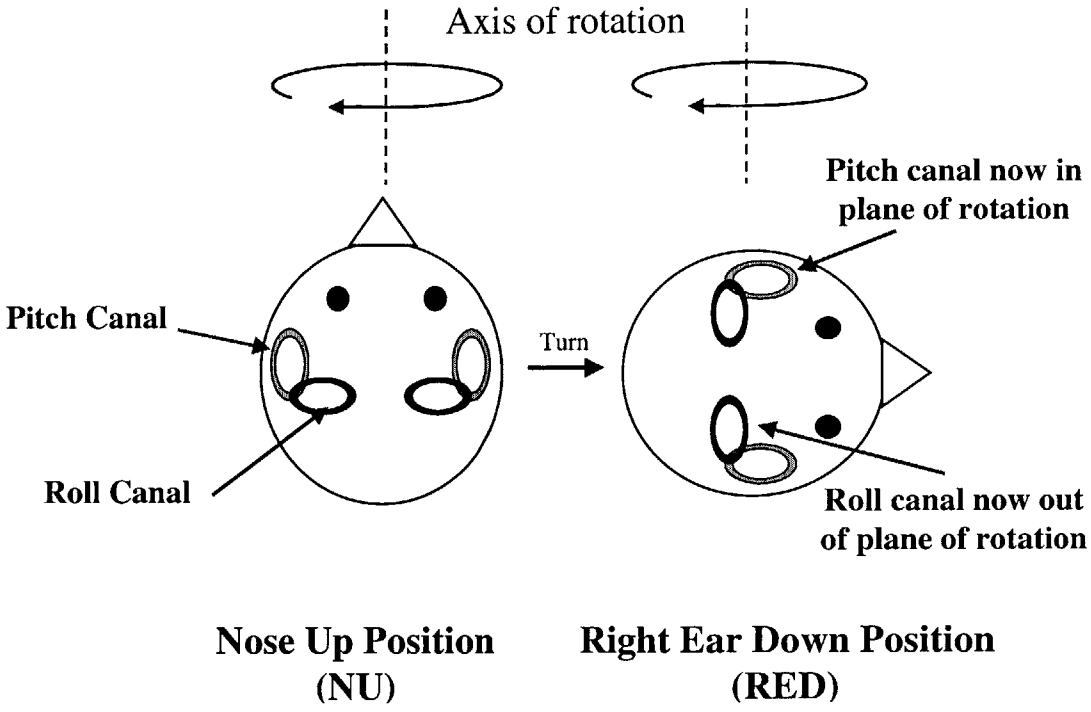


Figure 2.6 Diagram illustrating canals activated by a yaw movement during centrifugation (adapted from Sienko, 2002).

2.5.2 Head turn metrics

In studying the response to head turns, the essential metrics are the gain of the VOR, the VOR time constant, the illusions experienced, and the motion sickness elicited. The magnitude of these illusions and VOR are dependent on the rotation rate, and how much of the subject has turned the head. A faster centrifuge rotation rate will accelerate the semicircular canal more, and produce a stronger response in VOR gain and illusory sensation. Similarly, the greater the head turn, the greater the component of the canal that is introduced into the plane of rotation, and the greater the response.

2.6 Vestibular adaptation to centrifugation

Several studies have been performed on the 2 meter radius MIT centrifuge to show that adaptation to 23 rpm head-on-axis rotation is possible. Two studies are described in some detail below, since the protocols in these experiments is quite similar to the protocol used in this experiment.

The first study involved 8 subjects rotated in 20 minute sessions for 3 days. Each day the subject would perform as many yaw head turns as the subject was comfortable performing in the light (Young et al. 2001). This lights-on phase served as a habituation phase, and was compared with VOR and subjective experience measurements made in the dark before and after habituation. The same protocol was repeated on days 2 and 3. The results showed significant decreases in all measures, including amplitude of the VOR, the VOR time constant, and subjective ratings, across days and across pre and post adaptation phases. Additionally, at the end of the second day, "all measures had deceased by roughly one third of their initial magnitudes" (Young et al., 2001). Co-author Sienko used herself as a subject in the above protocol for 12 days, and at the end of the 12^{th} day motion sickness had disappeared entirely, but inappropriate eye movements did not (Sienko, 2000). This implies that the VOR may never adapt completely to cross-coupled stimulation.

In the second major experiment at MIT, the same protocol as above was followed, except 3 different visual surrounds were used (Brown et al., 2003). The three surrounds consisted of a stable non-rotating environment, an open rotating environment, and a completely dark environment. These alternative environments were meant to assess the influence of visual cues on the adaptation process and motion sickness scores. Subjects performed ad lib yaw head turns as before, although this time a period of commanded head turns in the light was also introduced. The results showed that the visual surrounding had no effect on motion sickness, but the two lighted-conditions had a significant effect on reducing SPV. The VOR time constant decayed significantly across pre and post habituation testing, showing indifference for all visual conditions. These

findings verify that retinal slip in the lit conditions is required to adapt SPV (Guedry, 1964), but not the VOR time constant.

2.7 The plasticity and transfer of adaptation

Several researchers have investigated the transfer of adaptation to one type of vestibular stimulus to other types of vestibular stimuli, also known as *generalization of adaptation*, or *learning to learn*. Guedry used a slow rotating room to test the transfer of adaptation to roll head movements made in one quadrant, to roll head movements in the opposite quadrant of the same plane (Guedry 1964, Guedry et al. 1964). Guedry rotated 32 men seated at 1.2 m from the axis of rotation at 7.5 rpm in the light, with half performing roll movements to the right, and the other half performing roll movements to the left (Guedry et al. 1964). Most subjects completed between 100-260 tilt-return cycles, comprising a habituation phase in the "practiced quadrant" for 4-5 hours. Nystagmus was recorded in the dark before and after the habituation period for roll head movements in both the practiced and opposite "unpracticed quadrant." The major finding was that while nystagmus amplitude and subjective illusory ratings declined after habituation in the practiced quadrant, there was little transfer of habituation to the unpracticed quadrant. In the same experiment, nystagmus was also measured during post-habituation head-static acceleration and deceleration of the rotating room, but no transfer of adaptation was observed.

The above studies imply that there is little transfer of adaptation between head movements in different quadrants of the same plane, but Guedry does suggest that "not enough post-habituation" measurements may have been made (Guedry 1964). That is, the initial impulse from the new stimulus may have been large, but subsequent turns may have yielded much lower VOR and illusory effects as the vestibular system learned to learn. Unfortunately, it is difficult to determine how many post-habituation head turns were performed in Guedry's experiments. The possibility that learning to accommodate a new stimulus requires a few head turns before taking effect is partially substantiated in another study by Guedry. In this study, nine subjects lived in a 2.4 m radius room

spinning CCW at 10 rpm for 12 days, and were free to move about and make voluntary head turns. Subjects also underwent pre and post habituation testing by making roll head turns on a rotating char in both CCW and CW directions. The results showed marked decreases in nystagmus amplitude for the post-habituation CCW chair testing, but movements performed for the CW chair rotation did not decrease below pre-testing levels. However, when measurements were made 2 days later, CW roll movement measures did decay substantially.

Two small studies on the MIT SRC have shown that habituation to yaw movements made in a single quadrant during CW rotation transfers to yaw movements made in the opposite quadrant, and to movements made in the same quadrant during CCW rotation. In the MIT 12 day adaptation protocol described in Section 2.6, Sienko also made head movements in the opposite quadrant (left ear down) at the end of the 12^{th} day (Sienko, 2000). These were "exceptionally stimulating", but the "estimated magnitude of the subjective responses decayed quickly with additional repetitions." Sienko also performed movements in the adapted quadrant while rotating the opposite direction, which were "extremely provocative", but also reported the quick decay of effects.

In a study by Brown, eight subjects were adapted to yaw head movements at 23 rpm over 3 days, and then covertly rotated in the opposite direction at the end of the protocol on a 4^{th} day. While the responses were significantly higher than the last measurements made on the 3^{rd} day, they were lower than the measures taken at the start of the 4^{th} day (Hecht et al., 2002). This result implies that adaptation between the two different inputs was successful, in contrast to Guerdy's quadrant transfer experiment.

Another study by Brown shows that changing the context in which head movements are performed does not influence the adaptation process. Brown had subjects adapted to yaw head movements over 3 days, and then relocated them to a slow rotating room at Brandeis University for days 4 and 5 (Hecht et al., 2002). Centrifugation rate and subject body position were held constant at the new location. The results showed that measures

of adaptation remained, implying that any contextual cues that may regulate adaptation were not located in subtle environmental changes.

Still other studies have assessed the problem of transfer between different environments, and different types of motion in that environment. In a study performed at the Pensacola rotating room, 2 military pilots that were highly susceptible to motion sickness were adapted to pitch and roll head movements over several months (Cramer et al., 1978). The subjects each performed 77,000 and 108,000 head turns at rotational rates between 0.25 rpm and 17 rpm. Each pilot, who had previously been grounded because of motion sickness, was subsequently able to complete flight training with no unusual incidents. While this study demonstrates transfer between environments, it does not imply transfer across canals since the pilots performed turns in all planes.

Finally, there is one study that found no evidence of transfer of adaptation between different planes. Tiliket et al. (1993) rotated subjects upright in a chair and trained the VOR gain up or down with a moving visual surround. Subjects were then pitched forward or rolled to one side by 45 degrees, and then rotated again with a moving visual surround. The changes in VOR gain that took place for the upright position did not appear to transfer to the new head tilted position. Additionally, when different subjects were first trained in the head tilted position, and then rotated in the upright position, the VOR gain still showed no transfer of adaptation. Tiliket suggested that these results imply that the vestibular system was taking cues from the otolith organs, and performing its motion calculations in "otolith coordinates."

2.8 Potential effects of gravity field on adaptation and VOR

Several studies have been undertaken to understand if head movements made while rotating in a microgravity environment are as provocative as they are on the ground. Data from the Skylab M131 Experiment, performed beginning on the fifth day in space, indicated that out of plane head movements made in a rotating chair did not cause motion sickness as they did on the ground (Graybiel et al, 1977). At least two parabolic flight

experiments have shown similar results, and found that motion sickness susceptibility during the 1.8 g portions of the flight was higher than at 1 g (Lackner and Graybiel, 1984; DiZio and Lackner, 1991). Another study by DiZio and Lackner (1992) showed that VOR time constants are reduced in weightlessness, which is again consistent with the model of velocity storage and motion sickness interaction (Section 2.4.2).

Nonetheless, there are at least three reasons why VOR and subjective responses should continue to be studied specifically in the context of SRC. The first is that when SRC is implemented the head may not be at the center of the centrifuge, and therefore the otolith organs would receive a linear acceleration cue analogous to gravity. This would especially be true for medium radius centrifuges. The second reason is that the gravity supplied by the Moon or Mars may not sufficient to inhibit the detrimental health effects of weightlessness that are seen on orbit. In this case, SRC may be an effective solution on the ground that would expose the user to a new gravity cue. The third reason is the rotation studies in done in micro-gravity so far have been too limited to make any concrete conclusions about the full human response to SRC.

Chapter 3 - Methods

3.1 Experiment design

3.1.1 Basic design

Subjects in this experiment will perform head movements while rotating at 23 rpm (1-G acceleration at the feet), clockwise when viewed from above, in the supine head-on-axis position (Figure 1.2). The head is always on center, but an adjustable footplate may be changed for subjects of different height, and thereby provide more or less than 1-G of acceleration at the feet. Figures 3.1 and 3.2 outline the protocol discussed below.

Subjects perform a block of 6 pitch head turns in darkness before and after a series of 24 yaw head turns. Subjective and physiological responses to the pitch turns before and after the yaw turns will be compared for evidence of adaptation. A portion of the yaw movements is made in the light to induce retinal slip, yielding a decrease in vertical (non-stabilizing) vestibuloocular reflex (VOR), slow phase velocity (SPV) amplitude, and time constant, τ. Data is collected during a block of yaw turns performed in darkness before and after the yaw head turns in the light in order to determine the amount of adaptation, Figure 3.1. The experiment is performed over two days to check for the effect of adaptation. Since signs of adaptation were observed in the pitch movements at the end of the experiment, a Control Group experiment without any yaw head turns was designed to determine to what extent yaw head movements influenced the observed pitch adaptation. The group that performed the yaw turns will be referred to as the Experiment group.

The protocol for the series of yaw movements in the Experimental Group, referred to as the Treatment, must be sufficient to invoke adaptation and habituation. The number of turns had to be provocative enough to elicit observable differences, but tolerable enough so that it could be completed even when performed in conjunction with the more provocative pitch movements. Pilot studies outlined in Appendix E attempted to

replicate lengthier but proven yaw adaptation protocols used by Sienko (2000), Brown (2002), and Lyne (2000) of this lab. Included in these previous experiments were allowances for *ad lib* head turns, where subjects performed between 25-60 turns on the first day, and more on the second and third days (Brown, 2002). Unfortunately, similar experiments when combined with pitch head turns were too provocative, and subjects would drop out due to motion sickness. Based on these findings, it was estimated that subjects could achieve a maximum of about 24 experimenter-directed yaw head turns, with a drop out rate near 50%. A compromise protocol was established that used no *ad lib* head turns, with 12 turns in the light, and 6 turns in the dark before and after the light phase.

The number of pitch head turns performed at the start and end of the yaw turns was chosen as a compromise between the risk of adapting the subject to pitch movements simply because of repetition, which could mask the effects of transfer of adaptation, and the need for statistically significant sample sizes. Additionally, inter-turn differences within a single block are scientifically interesting, there had to be a sufficient number. 6 pitch turns were chosen for the before and after blocks.

During the lights-on portions of the experiment, a stable non-rotating visual surround is presented to the subject by use of an opaque overhead canopy, Figure 3.3 and 3.4. Using a stable visual surround instead of an external rotating surround simulates likely operational SRC scenarios that may include reading, watching a display screen, or even using a virtual reality headset. Motion sickness and illusion intensity experienced in a stable visual surround have been shown to be no different from what is experienced in a rotating surround (Brown, 2002). The adaptive decrements of τ have also been found to not be statistically different. The opaque canopy also helps to eliminate light cues from the room during dark portions of the experiment.

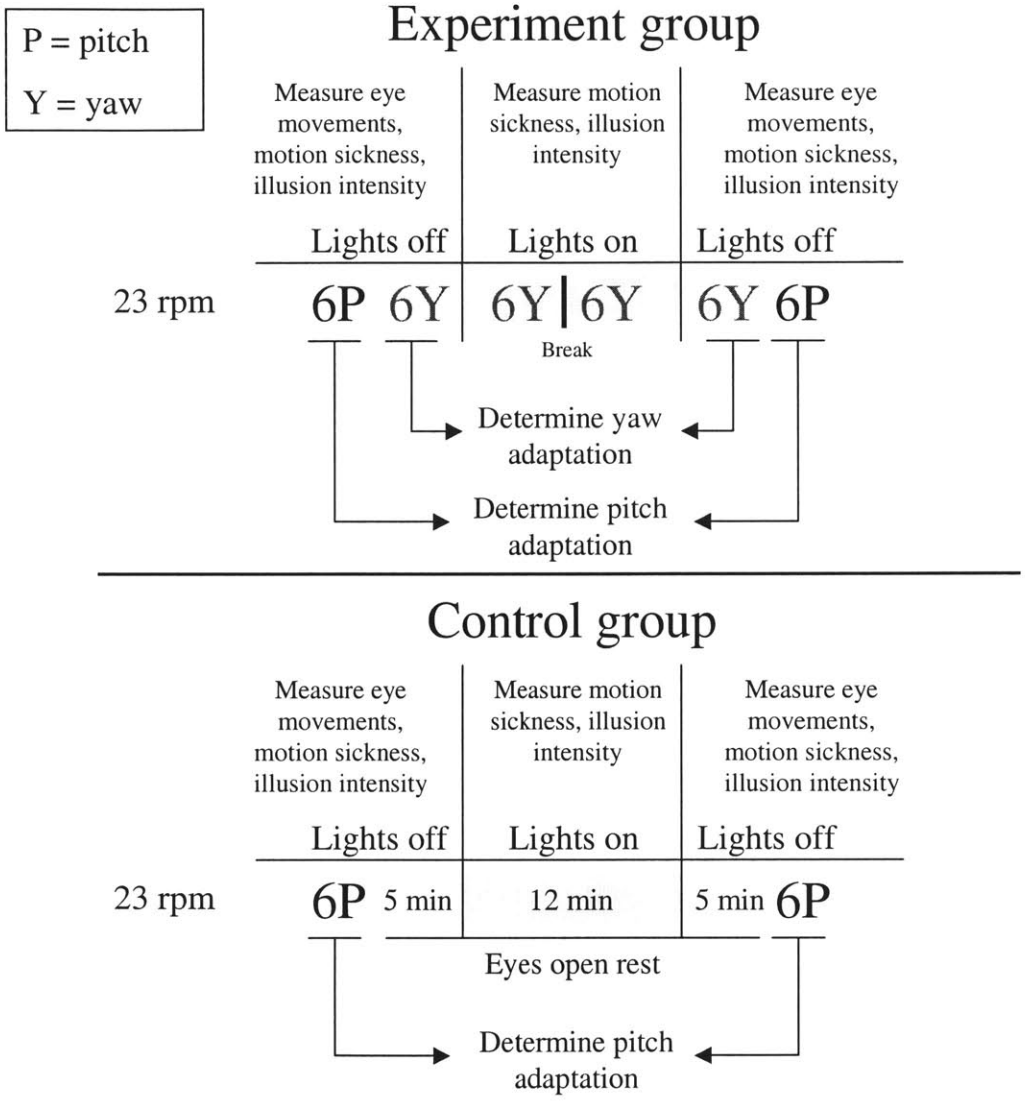


Figure 3.1 Experiment outline.

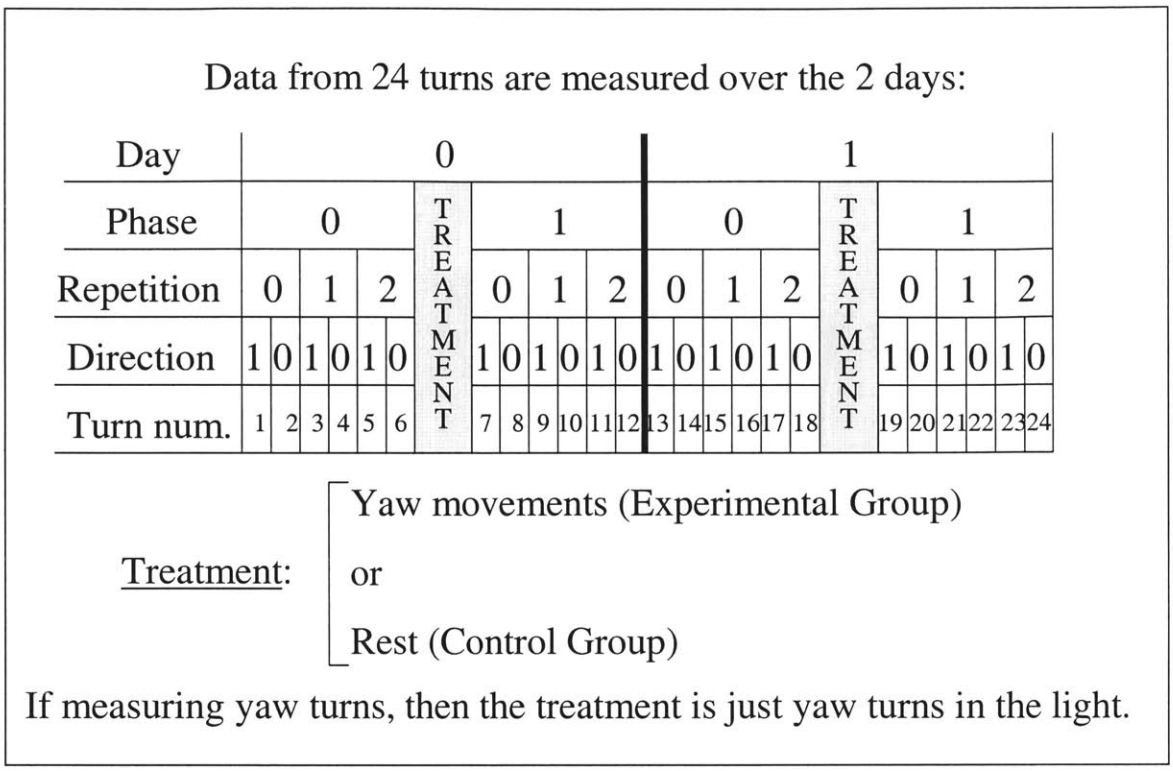


Figure 3.2 A diagram of the 24 head turns where measurements are taken, showing breakdown of the measurement groupings that are to be used in the analysis section.

3.1.2 Control group experiment

The Control Group protocol eliminates all of the yaw movements from the Experiment Group. This choice was balanced against eliminating just the yaw movements in the light, or just the yaw movements in the dark, which would have helped isolate if any cross-plane transfer was due to one of these yaw blocks in particular. However, eliminating all yaw movements provides a more definitive yes or no answer to the effect of yaw. If significant cross transfer is found, then a more detailed Control experiment can be designed. If not, then no further experiments are necessary. Eliminating just light or dark movements could find no transfer effect, which would still require another Control Group experiment.

3.2 Equipment

3.2.1 Centrifuge

The centrifuge used in this study is a 2 m radius "rotating bed" capable of spinning a single horizontal subject about the head or feet, Figure 3.3. The centrifuge is controlled by a 1 Hp motor, and is rated at a maximum speed of 30 rpm. The bed can accommodate subjects who are between 62 and 74 inches and weigh less than 200 lbs. An adjustable metal footplate at the end of the bed can be moved radially to assure that subjects of varying height will always be positioned with their head at the center of rotation. Safety features include metal gurney-style sidebars, an across the waist safety belt, and a subject operated emergency stop switch. For added safety, and to ensure the subject is complying with the experiment protocol, video monitoring is accomplished with an infrared camera. A 24 channel slip ring allows analog data to be collected from the bed, including the video signals. The rotator was built by Peter Diamandis, and a detailed description of its parts can be found in his MIT Master's Thesis (Diamandis, 1988).

For this experiment an opaque canopy is placed over the subject (Section 3.1.1), Figure 3.4. Three battery operated outdoor lamps are also placed on the interior of the bed and, when turned on by the operator, they provide the subject with a stable, non-rotating visual reference frame for retinal slip adaptation phases.

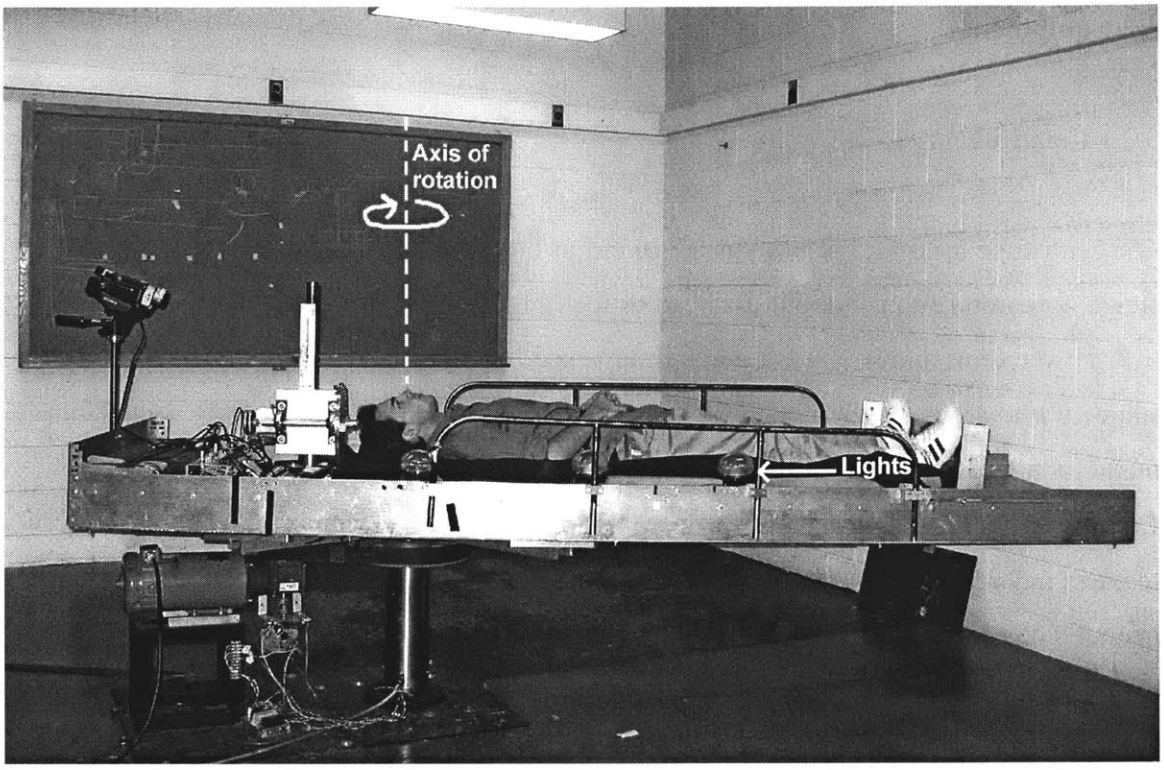


Figure 3.3 Centrifuge with three lights visible.

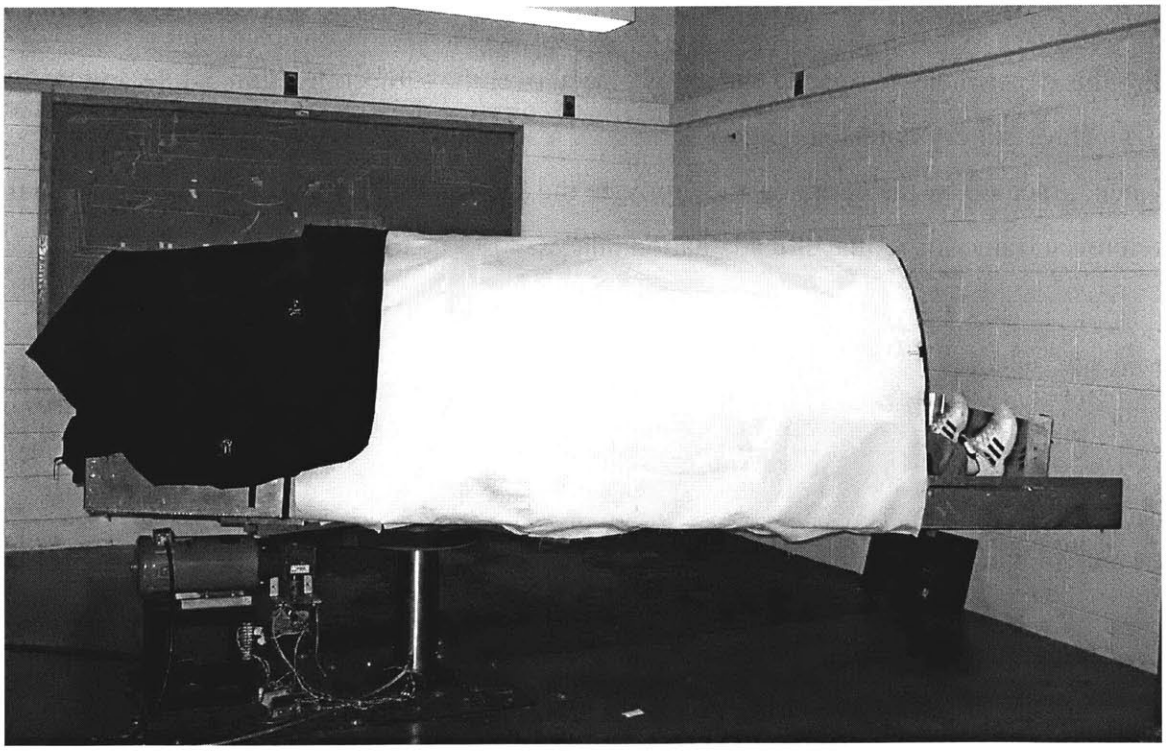


Figure 3.4 Centrifuge with opaque canopy.

3.2.2 Pitch head movement retainer

In order to constrain the subject's head motion in the pitch plane, an aviator cap fitted with a metal bar was used in conjunction with a stopping device located above the subject's head, Figures 3.5 and 3.6. The subject was instructed to move upwards until he or she felt the bar on the cap make contact with the overhead bar, and to maintain that position thereafter, Figure 3.7. A Velcro chinstrap on the cap ensured a snug fit and prevented slippage. For yaw movements, subjects were instructed to turn their head to the side as far as comfortable. A more precise method of constraining the subjects' movements would be to use a 2-axis yoke system, but it was found that with sufficient training and practice before the experiment, consistent movements could be made. See Section 3.5 for specific instructions issued to subjects on performing head movements with this device.

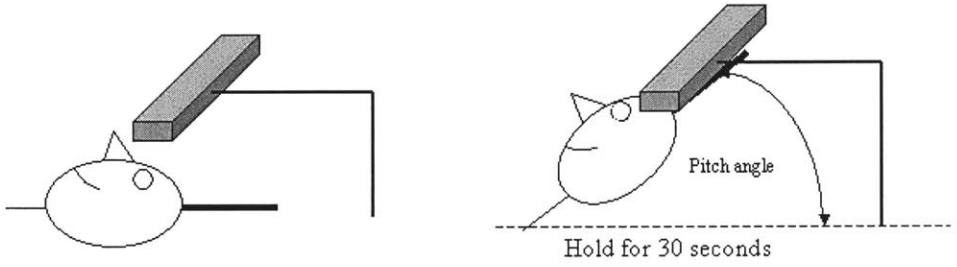


Figure 3.5 Method of ensuring consistency of pitch head turns.

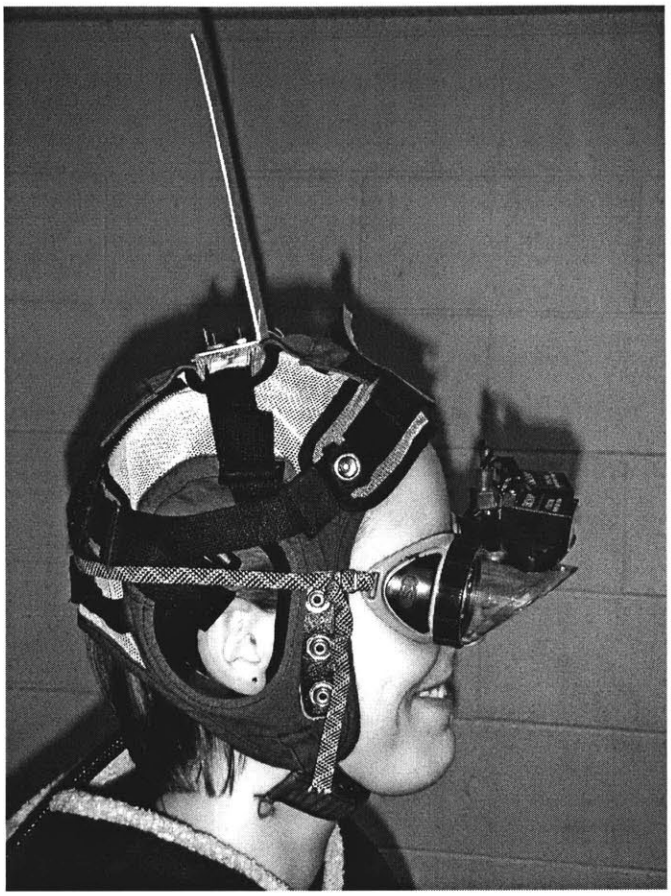


Figure 3.6 Profile view of the ISCAN imaging goggles along with the aviation cap and head motion restraint-rod.

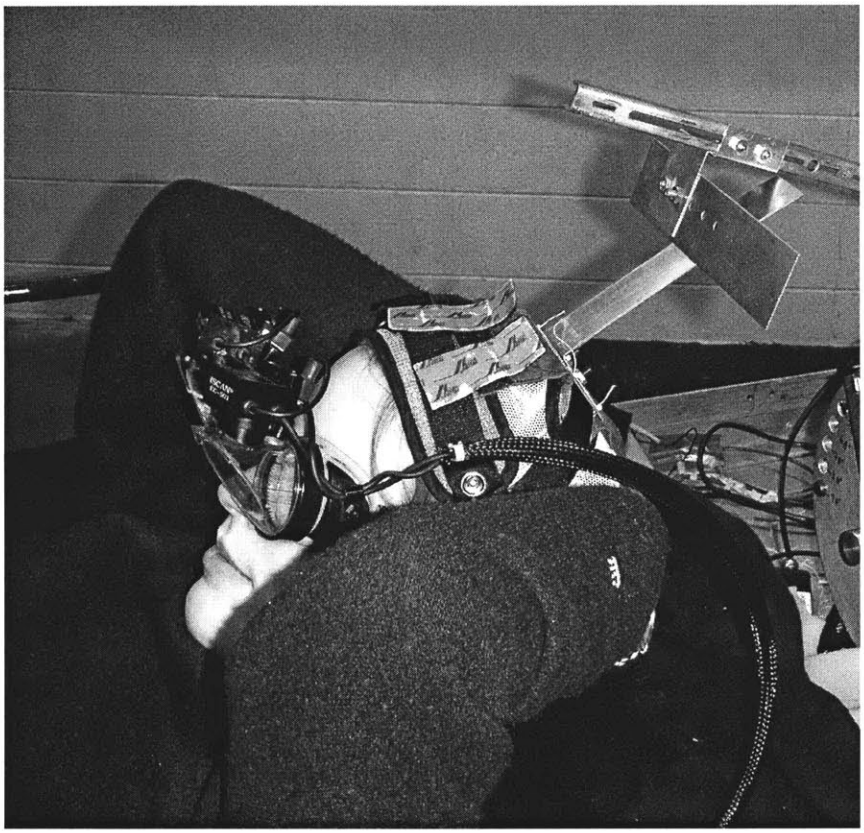


Figure 3.7 Subject demonstrating a pitch forward head turn (shown here without the blindfold). The subject is instructed to use their hands to stabilize their motions and to prevent neck and stomach muscle fatigue.

3.2.3 Eye movement recording goggles

Eye movement data was collected with ISCAN (Burlington, MA) Model RK-716PCI binocular goggle-mounted miniature video cameras and a small infrared LED illumination source. Light that enters the pupil is retro-reflected (travels directly back to the source), while the surrounding iris LED reflectance is diffuse, and the corneal reflectance is partially specular (usually visible as a small white dot near the pupil). The ISCAN video camera is off axis from the LED source, and so while it receives the reflected light from the iris and cornea, the retro-reflected light from the pupil merely appears as a dark spot. The video signal of the eye is transmitted to a desktop computer through the centrifuge slip ring, and processed using ISCAN software. The software finds the center of mass of the dark spot, which is assumed to represent the pupil center and approximate gaze of the subject. The contrast levels can be adjusted to ensure that a

proper lock is maintained. Typically, as the experiment progressed the contrast would have to be adjusted as the cross hair would become jittery and less stable on the pupil center. This increased jitter may have been due to heating of the camera electronics.

Calibration of the eye data coordinate system was accomplished by having the subject look at four dots a fixed distance above the head that were displaced from the center of vision by an angle of 10 degrees. A center dot was also provided to obtain the forward looking location of the eye, making a five point cross. Proper calibration of the goggles is essential for accurate velocity measurements. Special care must be taken to ensure that ISCAN has a lock on the center of the eye before its location is keyed in as a calibration point.

A cloth covering was also placed over the goggles when head movements were made in the dark to ensure that no light leaked in.

3.3 Subject recruitment and selection

Subjects were recruited primarily through posters placed around the MIT campus and respondents were typically MIT undergraduate and graduate students. Informed consent was obtained from 46 subjects who reported no neurovestibular problems, heart problems, eye problems, or low blood pressure, among other conditions (Appendix A). In the Control Group 3 females and 7 males, ages 19-41, finished out of 20 subjects, and in the Experimental Group 6 females and 4 males, ages 18-29, finished out of 24 subjects. Because the Experimental Group was completed first to test if a control experiment was needed (to see if there was evidence of any adaptation to pitch), subjects were not randomly assigned to the two groups.

Subjects numbered above 100 represent Experiment Group subjects, and subjects numbered below 100 represent Control Group subjects.

3.4 Measurements

3.4.1 Eye data

The recorded eye movements are analyzed for two primary values: the slow phase velocity (SPV), and the time constant of the decay of the slow phase velocity, τ. Here, the slow phase velocity is normalized by the rotation rate of the centrifuge and the angle of the head:

$$NSPV = SPV/ (138°/sec * \sin(\text{head turn angle in radians})).$$

The denominator represents the velocity component of the semicircular canals that is placed into or taken out of the centrifuge plane of rotation. This metric is similar to the gain of the VOR discussed in Section 2.3.1.

It is important to note that for yaw turns, following the transient during the head turn, the VOR motion will be in the vertical plane of the eye, while for pitch forward movements the VOR will be in the horizontal plane.

3.4.2 Motion sickness

Subjects were asked to report their motion sickness on a scale between 0-20, with 0 being normal, and 20 being about to vomit. Motion sickness rating was asked at least every minute for the Experimental Group, and after every head turn for the Control Group.

3.4.3 Magnitude of illusory sensations

During each head turn, subjects experience an illusory sensation of tumbling in space. Intensity of illusory tilt for all head turns is measured on a scale of 0-infinity, with the first pitch head turn having a baseline value of 10. The scale is linear so that a score of 20 is twice as intense as a 10.

3.5 Protocol

3.5.1 Pre-experiment procedures

Upon arrival at the lab, subjects were interviewed to make sure that they had none of the medically disqualifying conditions listed in Appendix A, including neurovestibular, neurological, and cardiovascular problems. Subjects also confirmed that they had performed moderate exercise semi-regularly, were within the weight limitations of the centrifuge, and had refrained from drug, alcohol, or caffeine use in the last 24 hours. Those subjects that met minimum requirements were explained the risks of the experiment, most notably motion sickness and the possibility of falling off the centrifuge while rotating. These risks were outlined in the consent form that the subject was instructed to read and sign before participating. The subjects were informed that they were free to drop out of the experiment at any time without penalty.

Consenting subjects were introduced to the centrifuge, its safety features, and the experiment protocol. The protocol was explained both verbally and through an instruction sheet (Appendix C). Awareness of motion sickness symptoms and illusory sensations was emphasized.

After lying down with the head-on-axis and donning the ISCAN goggles, the pitch movement head restraint bar was adjusted to provide the maximum amount of forward pitch that could be maintained for 30 seconds without being uncomfortable to the subject. The subject was also instructed to use both hands to support their head while performing the pitch maneuver to minimize left-right deviation, and to avoid working the neck and stomach muscles unnecessarily. The subject was also told to perform the maneuvers over 1 second. Once the subject was well situated in relation to the bar, the footplate was brought into place and the goggles were calibrated with the five-point target.

After calibration, the subject reviewed the pitch forward head movement by making a series of practice turns from nose up (NU) to nose forward (NF) to ensure consistency. After a consistent pattern was achieved, the subject's head angle while at the stop was measured with a protractor, using an imaginary line through the bottom of the subject's neck, ear, and top of the head. Yaw movements were then practiced at the maximum rotation angle that was comfortable to the subject. Again, after a consistent pattern of yaw movements were made, the angle of the subject's head was measured at RED with a protractor using the line through the center of the subjects eyes through the back of their head.

After these head turn practice routines, the canopy was added, the subject was told to place his or her blindfold on, and the room lights were turned out. Just before spinning, a final pitch movement and yaw movement were made to make sure no obstructions remained in the path of the aviator cap rod.

3.5.2 Experimental Group detailed order of operations

This protocol is performed identically on two consecutive days. As designed, the experiment should take about 29 minutes, but flexibility in the timing of head turns is allowed to accommodate the motion sickness of the subject. Note that "phases" listed here do not correspond to the Phase factor used in the analysis.

Yaw head turns: each yaw maneuver to RED or NU is performed over 1 second, and head movements are separated by 45 seconds.

Pitch head turns: Each pitch up or down maneuver is performed over 1 second. Pitch forward head movements are held for 30 seconds, and upon pitching back the subject waits for 1 minute before pitching up again.

Phase 1 – Ramp up to 23 rpm in darkness – 30 seconds. Inquire motion sickness.

Phase 2 – 6 timed and commanded pitch turns in darkness. *Measure*: inquire motion sickness and illusion intensity after 10 seconds, record eye movements.

Phase 3 – 6 timed and commanded yaw turns in light. *Measure*: inquire motion sickness and illusion intensity after 10 seconds, record eye movements.

Phase 4 - 6 timed and commanded yaw turns in the light with the blindfold removed. *Measures*: inquire motion sickness and magnitude of illusory sensation.

1 minute mandatory break

Phase 4 - 6 timed and commanded yaw turns in the light with the blindfold removed. *Measure*: inquire motion sickness and magnitude of illusory sensation.

Phase 5 – same as phase 3.

Phase 6 – same as phase 2.

Phase 7 – ramp down to 0 rpm over 30 seconds and debrief subject.

3.5.3 Control Group order of operations

Again, the protocol is performed over two days. It is designed to last 32 minutes, based on the results of the Experiment Group, although flexibility for longer inter-turn breaks is allowed for motion sickness. The turn protocols are the same for this group as for the Experimental group.

Phase 1 – Ramp up to 23 rpm in darkness – 30 seconds. Inquire motion sickness.

Phase 2 – 6 timed and commanded pitch turns in darkness. *Measure*: inquire motion sickness and illusion intensity after 10 seconds, and record eye movements.

Phase 3 – 5 minutes of eyes open darkness exposure. Monitor motion sickness.

Phase 4 – 12 minutes of eyes open light exposure. Monitor motion sickness.

Phase 5 – 5 minutes of eyes open darkness exposure. Monitor motion sickness.

Phase 6 – same as phase 2. Monitor motion sickness.

Phase 7 – ramp down to 0 rpm over 30 seconds and debrief subject.

3.5.4 Post-experiment

After the experiment is complete, ISCAN data is saved in coded ASCII text files for eventual processing.

Chapter 4 – Eye Data Analysis

4.1 Eye data analysis

4.1.1 Software package

Calibrated eye data from the ISCAN software is saved in ASCII tables that contain left and right eye positions in degrees for the horizontal and vertical axes, sampled at 60 Hz. These files were read into the Matlab software environment using a data processing software package modified from what has been used for other MIT experiments (Appendix G, and Sienko, 2000). Left eye movements were used except in instances where there was a significantly cleaner signal for the right eye.

Some of the original 24 Matlab "m-file" routines used in this package were written as scripts that output their variables into a common workspace. Since using scripts permits variables of the same name to be overwritten by other variables, contamination is possible, and adding new m-file routines is more difficult. To update all of the software for easier additions, and for easier understanding, almost all scripts were turned into Matlab functions. Additionally, some extraneous code was eliminated and more in-line documentation was added. The new version of the code is contained in Appendix G.

4.1.2 Data processing

Once the eye data has been read into Matlab as arrays, the position data is first filtered with several passes of Butterworth and order statistic (OS) filters to remove noise and blinks (see file *batch_eye_channel.m*). The filtered positions are then differentiated and the slow phase velocity is extracted with an adaptive asymmetrically trimmed-mean (ATTM) OS filter. The ATTM OS filter works by sliding a window across the velocity data, ranking the data samples and sorting them in ascending order. Based on the assumption that the eye spends more time in the slow phase than in the fast phase, the

resulting distribution should be skewed towards the slow phase velocity. The filter calculates the skewness of the velocity distribution based on the minimum, maximum, and median, after "trimming" some of the beginning and end values. The filter then delivers an estimate of SPV at the center of the window based on skewness and properties of the distribution. These SPV values are collected as the window moves over the data, and are linearly interpolated to give a final plot of SPV. David Balkwill was responsible for writing many of these routines, and details of the process can be found in (Balkwill, 1992).

4.1.3 Exponential fit

As discussed in the Background Section, the decay of the SPV can be described by an exponential decay,

$$A\exp(-t/\tau),$$

where A is the amplitude, and τ is the time constant. In the past, curves were fit with an automated routine (*eye_anal.m*) that scanned through the data and found the start of the curve. For this study, all curves were fit manually by visually inspecting the curve (using *eye_anal_manual.m*), starting the fit at the highest SPV, and ending it where the velocity fell to zero. This time was typically 5-15 seconds for yaw head turns, and 20-30 seconds for pitch head turns. A regression-based curve fitting procedure was used to find the curve. The goodness of fit for the curve was based on the ratio of the regression mean square error to the residual mean square error, or F value. All regressions had F values much greater than 3, which corresponds to significance at the $p > 0.05$ level. Examples of these fits can be seen in Figure 4.1, which also show the change in time constant as adaptation takes place.

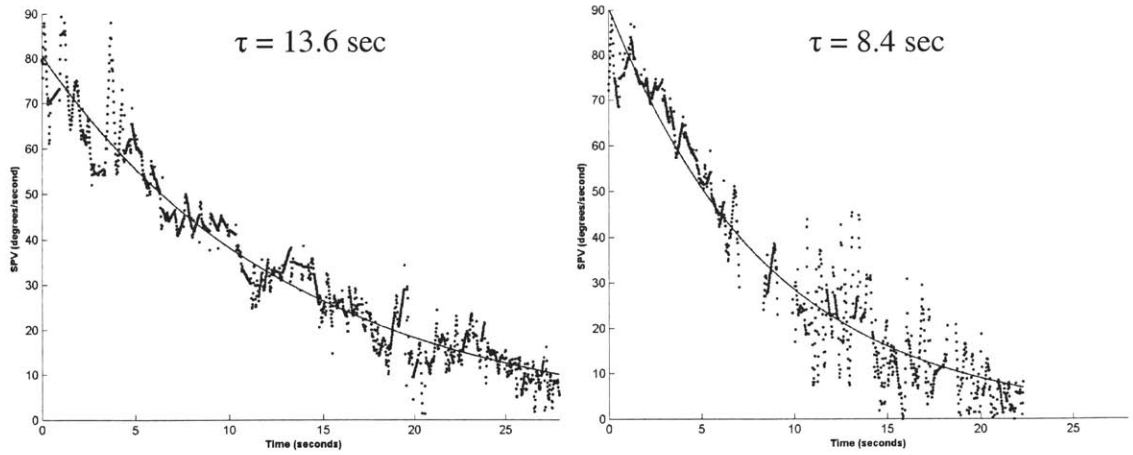


Figure 4.1 Curve fits for a subject before and after adaptation, each showing a reduction in τ HVOR (Subject 116 pitch turns: left, Day 0, Phase 0; right, Day 1, Phase 1).

4.1.4 Noise elimination routine

It was frequently found that some noise, possibly artifacts of blinks, remained after filtering. This noise often appeared as regions of speckled points between the curve and the x-axis, Figure 4.2a, or as clear spikes, Figure 4.2b. Noise generally increased as the experiment went on. Since this type of noise was easily identifiable by eye, yet was distorting time constants by several seconds, it seemed worthwhile to find a way to eliminate it.

A program (*data_eliminator.m*) was developed that would enable the user to draw an arbitrary shape around noise, delete it while maintaining the time information in original plot, and then proceed to fit the data. The algorithm is based on the idea that for any arbitrary closed shape around a point, an infinite line passing through that point will also pass through an odd number of shape sides on one side of the line. If the point is outside the shape, then an infinite line will pass through an even number of shape sides on one side of the line, or no sides at all, Figure 4.4.

The user draws a shape around the noise by clicking the mouse and the program generates a shape model by connecting the points. The program then creates horizontal

lines through all of the nearby data points to determine how many times they pass through the shape's sides. Points inside the shape are deleted. A detailed explanation of the algorithm is found in program's heading, which is contained in Appendix G with the rest of the analysis code. Figure 4.4a and 4.4b show the improvement after removing the noise in Figure 4.3. The difference in τ values before and after eliminating noise is above the mean difference observed before and after adaptation for all pitch movements (see Figure 5.18). Therefore, it is possible that this algorithm could help small studies obtain statistically significant results.

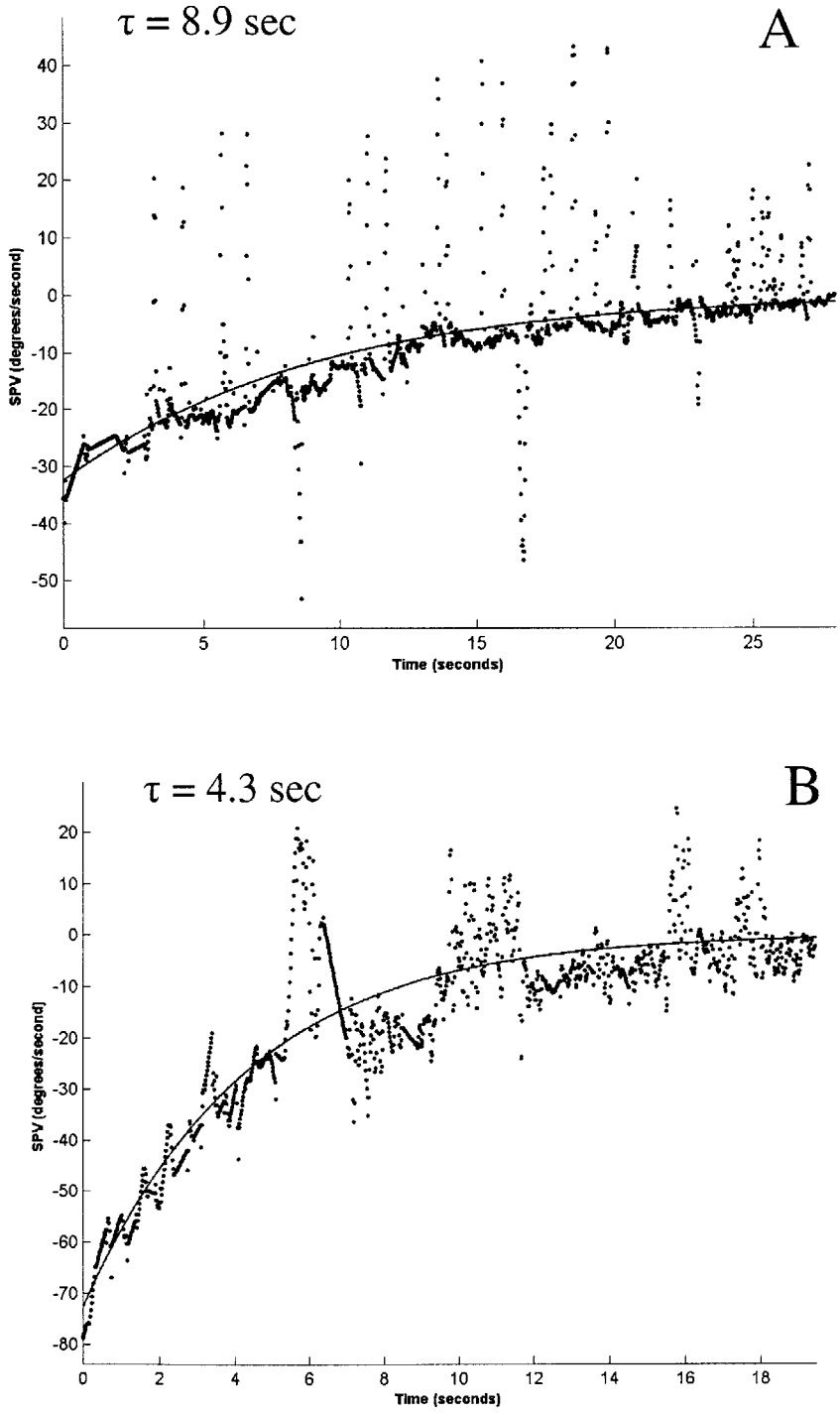


Figure 4.2 Two examples of typical noise found in approximately 25% of head turns. A, diffuse noise (subject 24, pitch, second day, phase 0, turn 3), and B, spikes (subject 15, pitch, second day, Phase 1, turn 5).

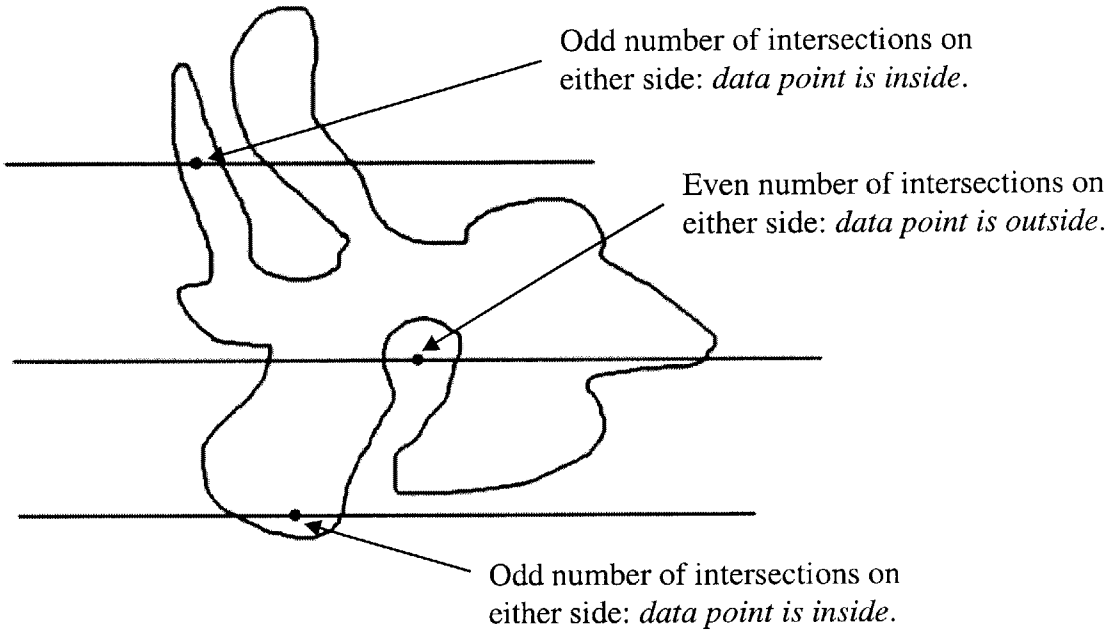


Figure 4.3 Algorithm for editing data on the fly by drawing a shape around unwanted data and eliminating it. A horizontal line (or arbitrary line) passing through a point inside an arbitrary closed shape must intersect the shape's walls an odd number of times on each side of the line. For points outside the shape, a horizontal line will intersect an even number of walls on each side, or no walls at all.

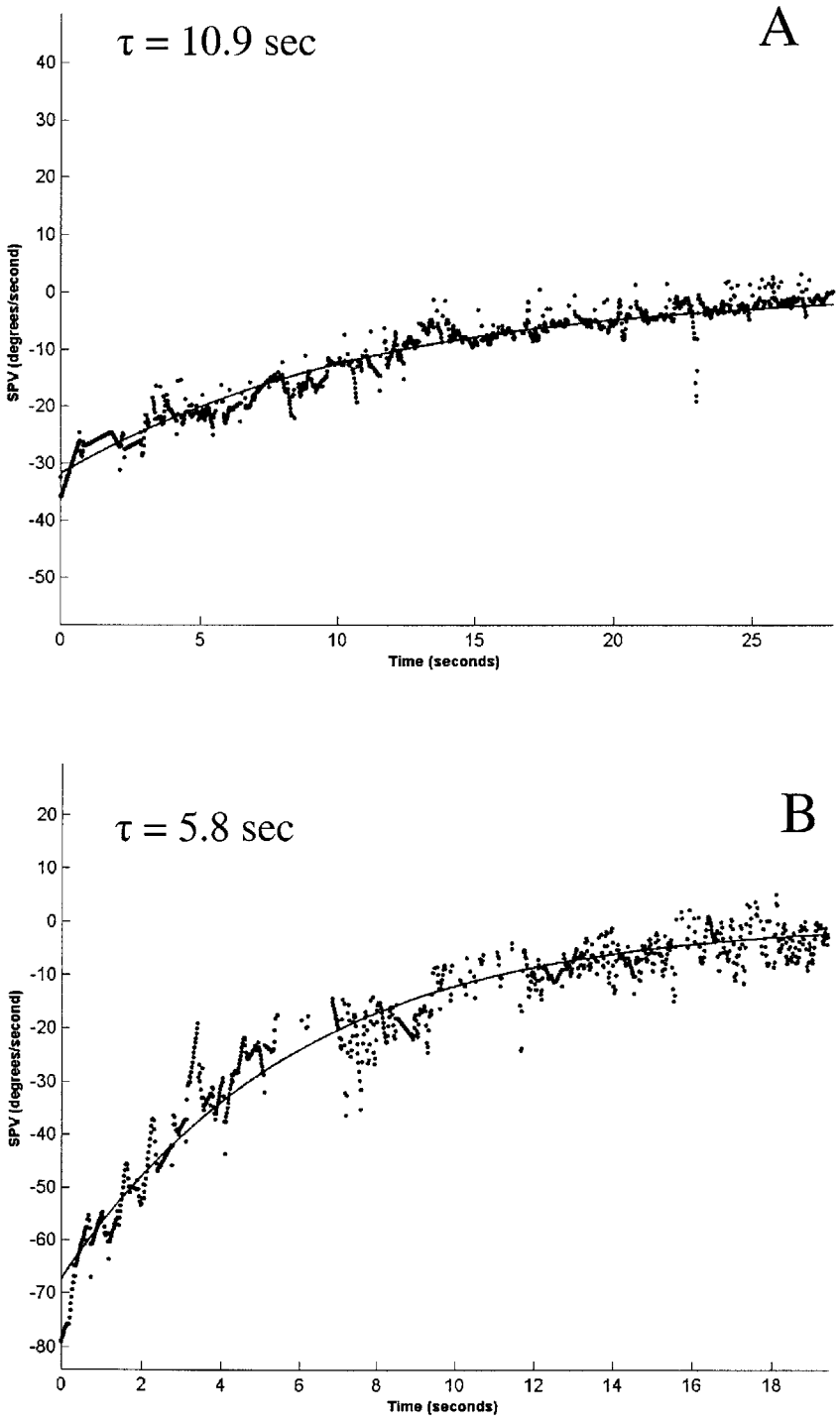


Figure 4.4 Curve fits of the data in Figure 4.2 after manual removal of noise. Statistical significance of the curve fits tripled in each case.

Chapter 5 - Results

5.1 Overview

The General Linear Model (GLM) univariate repeated measures ANOVA of the SYSTAT software package (v. 10, Systat Software Inc., Richmond, CA) is used to test for significant effects at the $p < 0.05$ level. The p values are Huynh-Feldt corrected where applicable. When viewing graphs of the data, it may be helpful to refer back to Figure 3.1 and Figure 3.2, which show how the conditions Day, Phase, Rep, and turn Direction are organized. Most graphs show mean values with standard errors, unless otherwise noted.

In Section 5.2, a summary of motion sickness and drop out rates is presented. Most subjects dropped out while performing pitch head turns in the second Phase of the first day. For the Experimental Group, motion sickness generally increased within a Day, but declined between the two Days.

The results of the yaw movements are presented in Section 5.3. For the yaw movements we expect to find evidence of adaptation based on previous studies, and indeed we find it. Vertical VOR τ values decreased over Days ($p = 0.017$) and Phases ($p = 0.001$), and slow phase velocity normalized to the head turn angle (NSPV) decreased over Phases ($p = 0.0005$), but not over Days. Illusory motion intensity decreased by Day ($p = 0.014$) and Phase ($p = 0.004$). If we had not found evidence of yaw adaptation, it would be difficult for us to claim that adaptation had transferred from yaw to pitch movements, should that finding emerge.

Data from the pitch movements in the Control and Experimental Groups are presented in Section 5.4. Evidence of adaptation to pitch movements is assessed globally for both Groups, and appears in significant decreases of the horizontal VOR (HVOR) τ values by Day ($p = 0.0005$) and Phase ($p = 0.0005$). Illusory sensations decreased over Days ($p =$

0.001). The only main effect found to influence HVOR NSPV was a difference in turns nose up (NU) to nose forward (NF), and from NF to NU, which is not necessarily a consequence of adaptation.

The data have also been analyzed for any differences in adaptation patterns between the two Groups that may have been caused by the yaw movements. All but one of the significant between-Group differences are cross effects involving turn Direction. The exception is in the NSPV variable, effect of Group*Phase*Rep ($p = 0.024$). Two five-way cross-effects of Day*Phase*Rep*Direction*Group are found for both the τ ($p = 0.039$) and illusory ($p = 0.044$) variables, but these effects can largely be dismissed as artifacts, with their origin in single anomalous measures. No effects of Day*Group or Phase*Group were found.

As stated in the Methods Section, subjects in the Experimental Group have subject numbers greater than 100. Subject 102 was excluded from all analyses because his values for τ during pitch movements were irregular and inconsistent with those for the rest of the subject group. When included, the subject produced statistically significant effects in the pitch movement analyses that were not observable in the rest of the subject pool, and which disappeared when his exceptional results were excluded

5.2 Drop outs and motion sickness (MS) for all head turns

Table 5.1 shows where subjects dropped out of the experiment. Not all drop outs are included, since some of the subjective metrics data files for drop outs were lost when a computer crashed. Despite carefully monitoring motion sickness scores after almost every head turn, three subjects came very close to vomiting in the middle of practicing the second set of pitch turns on the first day. In such instances, the motion sickness scores were low to moderate, but the subject seemed to become sick very quickly over the course of one pitch head turn. One subject started to retch after pitching forward, even though the motion sickness score was an 8 prior to the turn. Another subject claimed to have vomited and swallowed it, and then said again later that he didn't really

vomit at all, probably out of embarrassment. A third subject verbally indicated he was about to vomit, but didn't. Sometimes, a particular turn from NU to NF would be very provocative, but that subject would have to come back down to rest and experience another turn before stopping. Subjects were offered the chance to stop spinning with their head up, but only one subject accepted the offer.

Table 5.1 Summary of most subject drop outs due to motion sickness.

Subject	**Where stopped**	**Last two MS scores**	**Comments**
Control			
2	Day 0, Phase 0, 2nd turn	3,10	
3	Day 0, Phase 0, 2nd turn	10,13	
4	Day 0, during rest with lights on	5,10	MS grew during rest
5	Day 0, Phase 0, 2nd turn	10,15	
6	Day 0, during rest with lights on	10, 10	MS grew during rest
9	Day 0, during rest with lights on	13, 15	MS grew during rest
14	Day 0, Phase 0, 4th turn	8, 10	Very sick
Exp.			
101	Pitch, Day 0, Phase 1, 2nd turn	6,6	
104	Pitch, Day 0, Phase 1, 4th turn	15,15	Subject was encouraged to stop
107	Pitch, Day 0, Phase 0, 4th turn	1, 10	
109	Yaw, Day 1 last yaw turn in light	1, 2	Was "uncomfortable"
117	Yaw, Day 0 last yaw turn in turn	9, 9	
119	Yaw, Day 0, 3rd yaw in light	5, 6	
122	Pitch, Day 0, Phase 1, 2nd turn	9, 15	
123	Pitch, Day 0, Phase 1, 2nd turn	5, 6	
125	Pitch, Day 0, Phase 1, last turn	10, 20	Did not return for Day 1

The highest motion sickness scores achieved within blocks of six head movements are plotted for both Days in Figure 5.1. The Control Group only performed 2 blocks of pitch movements per Day, and so there are only four data points. Generally, it is clear that motion sickness rose with successive head turns, and did not plateau. For the Experimental Group motion sickness was lower on the second day compared with the first (paired t-test, $p = 0.005$), indicating adaptation had taken place to some extent. For the Control Group, the errors are too great to make any conclusions.

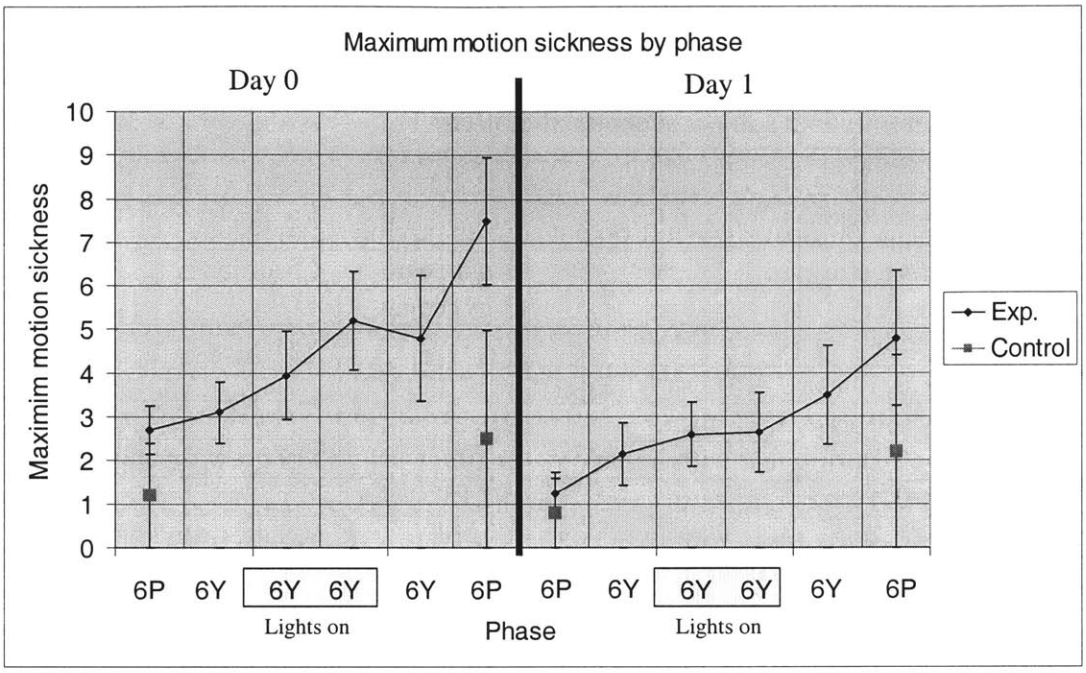


Figure 5.1 Maximum motion sickness scores achieved in each Phase on both Days.

5.3 Yaw head turns

5.3.1 Significant effects

Subjects performed yaw movements that ranged from 65-85 degrees. A typical plot of SPV for 6 movements is shown in Figure 5.2. Table 5.2 shows a summary of the significant effects from the ANOVA analysis.

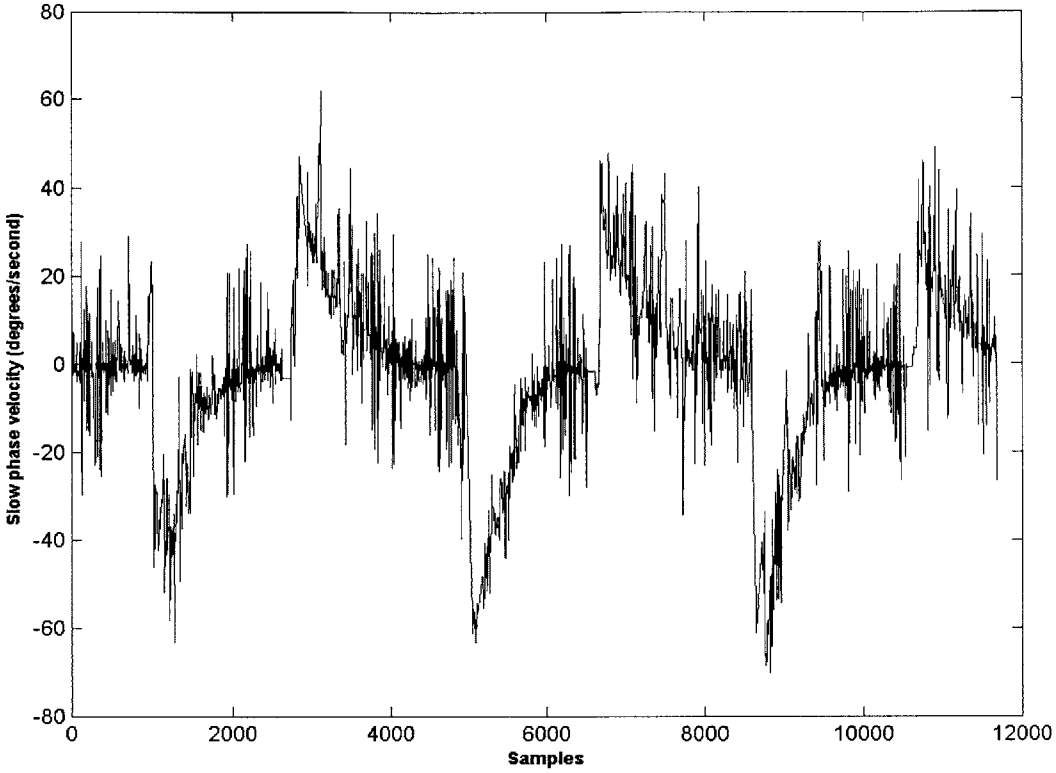


Figure 5.2 Typical block of 6 yaw turns (Subject 103, first Day, first Phase).

Table 5.2 Summary table of significant effects in the yaw turns performed by the Experimental Group at the p = 0.05 level.

Variable	**Day**	**Phase**	**Rep**	**Turn Direction**	**Cross effects**
Tau	F(1,7) = 9.777, p = 0.017	F(1,7) = 33.586, p = 0.001			
NSPV		F(1,7) = 94.779, p = 0.0005		Trend	Day*Rep (F(2,14) = 4.98, p = 0.023)
Illusory sensations	F(1,7) = 10.586, p = 0.014	F(1,7) = 17.884, p = 0.004		F(1,7) = 14.641, p = 0.006	

5.3.2 – Yaw head movement time constant (τ) values

A histogram of yaw τ values from the vertical VOR is presented in Figure 5.3, which shows the data are approximately normally distributed with a mean of 4.7 seconds.

The graph's results are comparable to results obtained by Sienko (2000) and by Brown (2002), Figure 5.4, which helps support the claims of the current experiment. Note that this single exponential τ estimate includes both the underlying cupula time constant and the central one.

The τ values for each yaw head turn are presented in Figure 5.5. Of the total of 24 recorded head turns, the first 12 were on Day 0, and the second set of 12 were on Day 1. Each of the Days is broken into two Phases of 6 turns each, and between those Phases subjects perform 6 turns in the light (refer to Section 4.3 and Figure 3.2). The results of the 24 turns are displayed consecutively to make it easier to appreciate the overall trend by Day and Phase. Much of the data will be presented in this 24-trial format.

Most notably, there is a significant decrease in τ both by Day ($p = 0.017$) and Phase ($p = 0.001$). The τ value trend is slightly erratic, but some of the strong peaks are partly due to differences between individual subjects. Removing any single subject, including the outlying Subject 102, does not, however, change the statistical significance of any of the results in Table 5.1, or the observed general trend. This supports the belief that we have a coherent pool of subjects and that the statistically significant results represent them reliably.

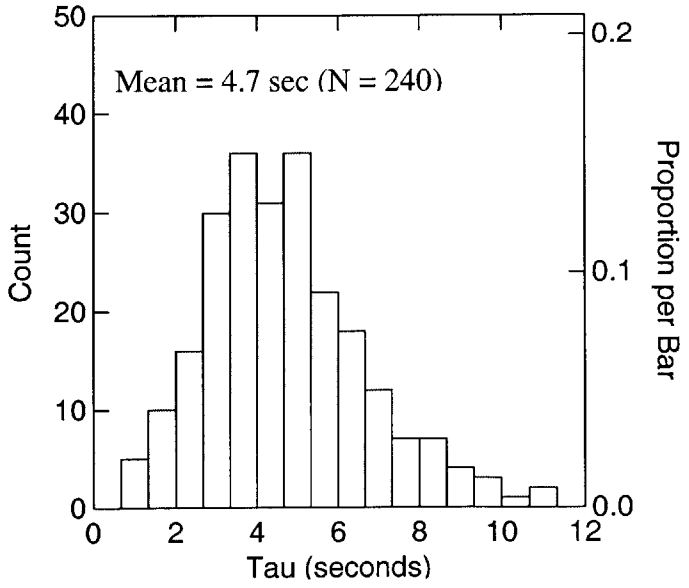


Figure 5.3 Histogram of τ values for yaw head turns.

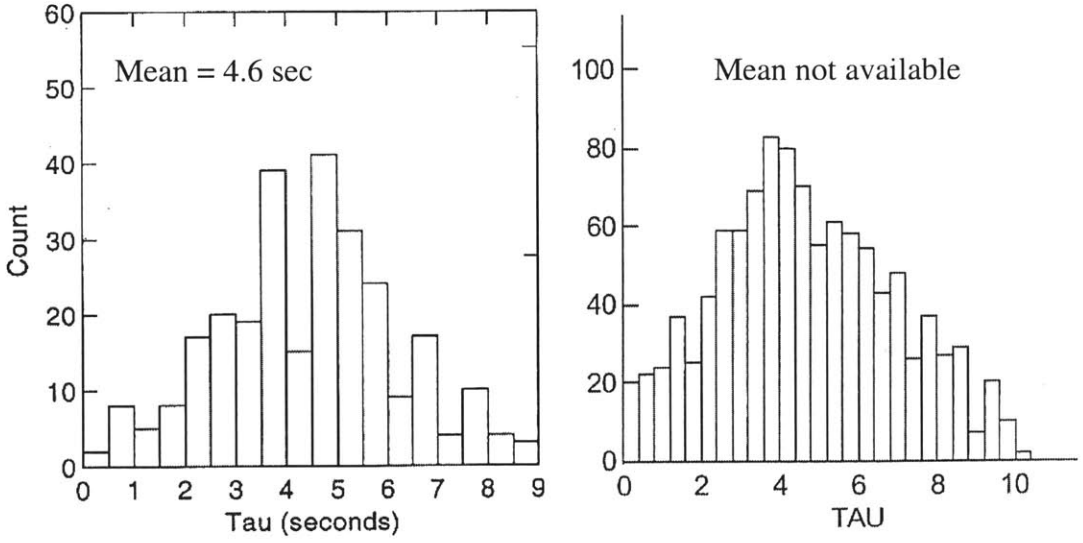


Figure 5.4 Histograms of τ values for yaw head turns, taken from Sienko (2000), left, and Brown (2002), right, both of which are consistent with the histogram in Figure 5.3.

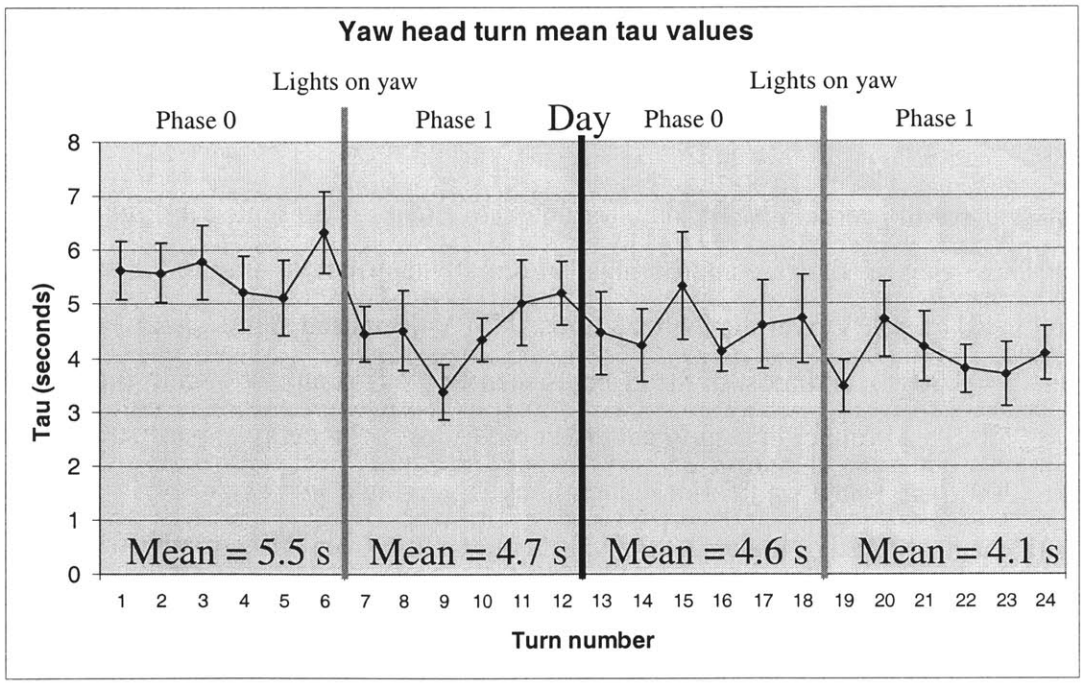


Figure 5.5 Mean τ values of vertical VOR for yaw head turns. A significant decrease in τ is found both by Day and Phase.

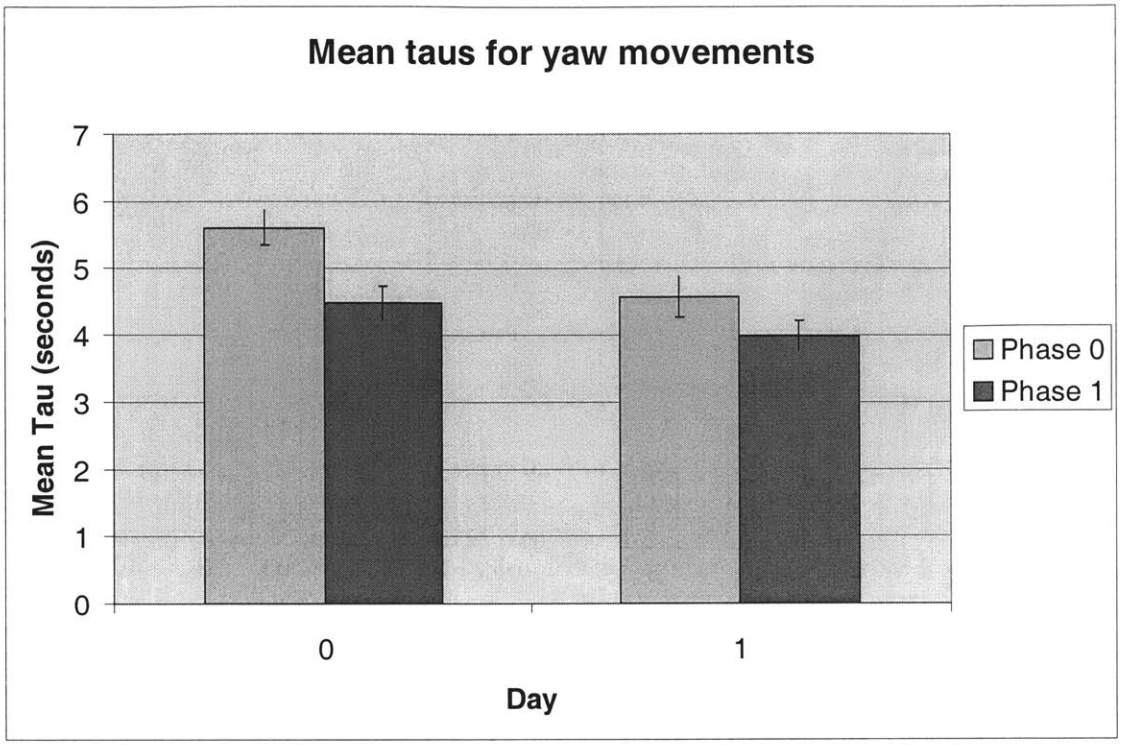


Figure 5.6 Decrease in τ VOR for yaw turns over Days and Phases.

5.3.3 – Normalized slow phase velocity

A histogram of the vertical NSPV data for yaw movements is presented in Figure 5.7, which shows that the data are approximately normally distributed. Figure 5.8 shows the general trend of NSPV over the 24 head turns. NSPV decreased significantly between Phases ($p = 0.0005$), and most of the effect is seen on the first day, shown in Figure 5.9. Brown (2002) also found no significant effect of Day for a three day experiment, but Sienko (2000) did find a significant reduction by Day using a similar protocol. The data also show a clear trend of higher NSPV values on the turn from RED to NU (which is also visible in the sample data, Figure 5.2) than on the turn from NU to RED. The effect was not, however, statistically significant in the GLM analysis.

Figure 5.9 shows the mean values for each turn direction. The absolute magnitudes between 0.3 and 0.35 agree with the results of Newby (2002). Brown (2002) and Sienko (2000) find, however, that turns from NU to RED yield higher NSPV values than turns

from RED to NU. The cause of the discrepancy with this study is not clear, but it is notable that the higher NSPV scores in this study are in phase with the higher measured illusory intensity scores (from RED to NU). Brown (2002) and Sienko (2002) found the reverse; their subjects' illusory sensations were greater in the head turn direction for which NSPV was smaller.

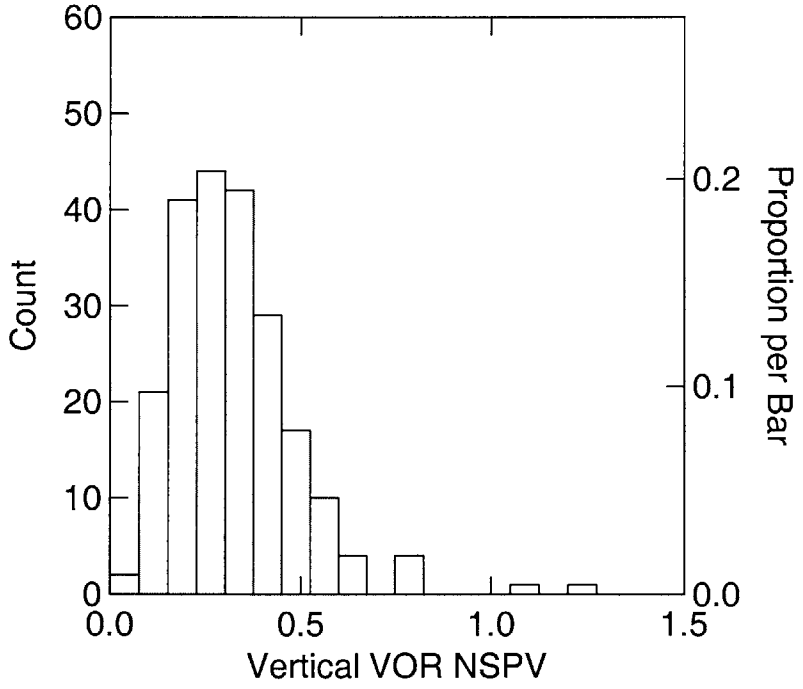


Figure 5.7 Histogram of vertical VOR NSPV values for yaw head movements.

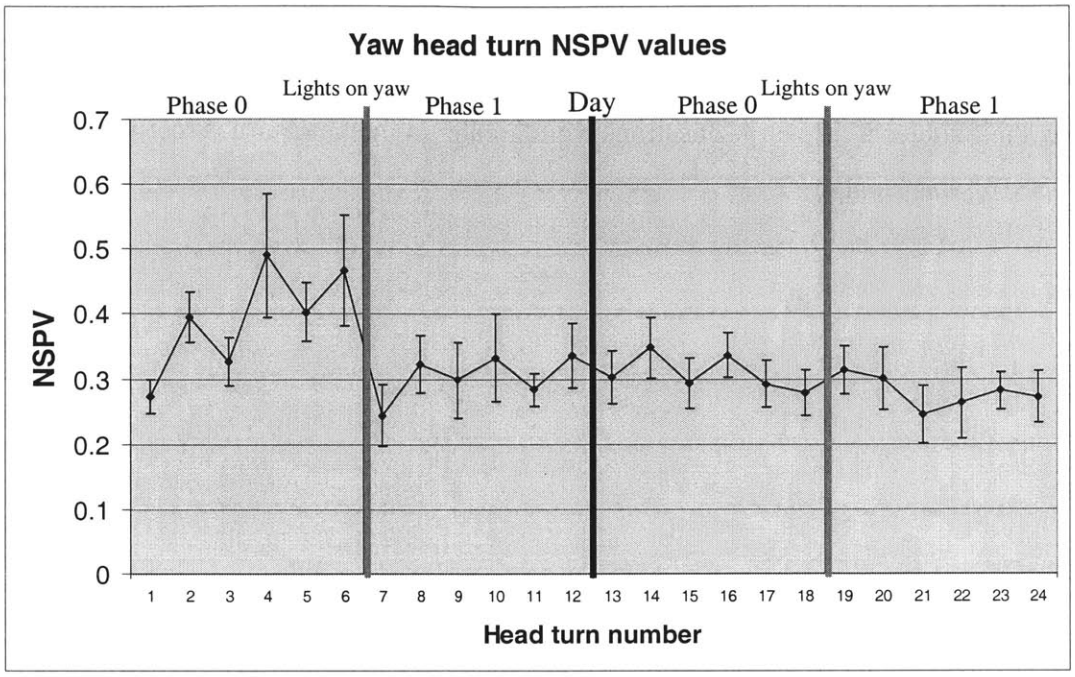


Figure 5.8 Vertical VOR NSPV values measured during yaw head turns.

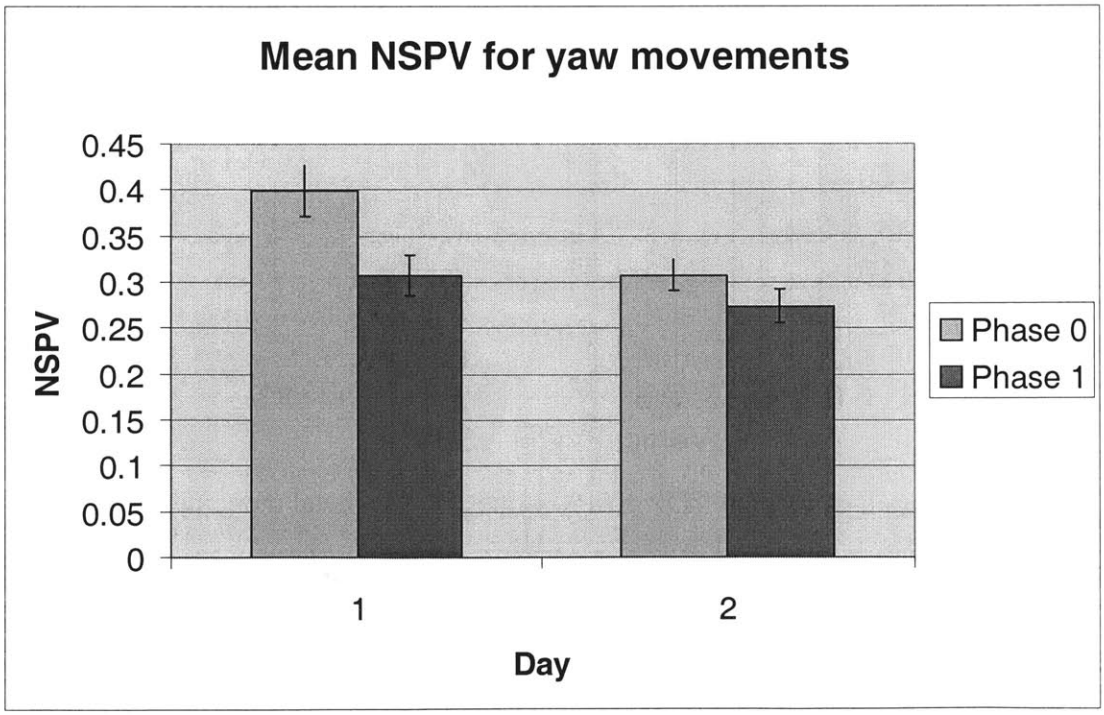


Figure 5.9 Effect of Phase and Day on vertical NSPV for yaw movements.

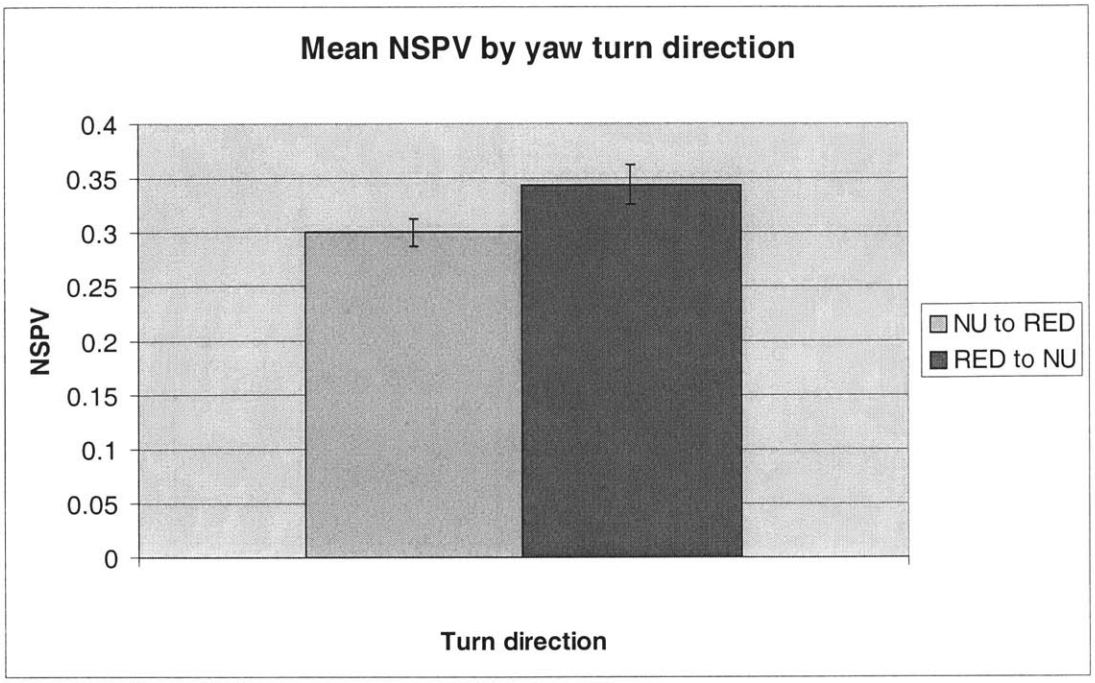


Figure 5.10 Difference between NU to RED head turns and RED to NU. While the difference is not statistically significant, the trend is visible in Figure 5.8, and the difference is the opposite of what is found by other investigators.

5.3.4 Illusory intensity

As the subject's head is rotated in the yaw plane, they experience illusory sensations of tumbling and spinning, predominantly in the pitch direction, which they rate on a linear scale anchored to 10 (Section 3.4.3). These subjective scores of illusion intensity declined significantly over Days ($p = 0.014$) and Phases ($p = 0.004$), Figure 5.11. The distinct sawtooth pattern also shows that turns from NU to RED produce less of a pitch illusion than turns to NU ($p = 0.006$), which agrees with past research. The mean difference between directions was about 3 rating points, Figure 5.12, compared to about a 1.5 point difference observed by Newby (2002). The difference between illusory sensation on RED and NU turns in the last phase seems to diminish, implying a Day*Phase*Direction effect, but it is not significant, possibly because of the higher standard error in the final phase.

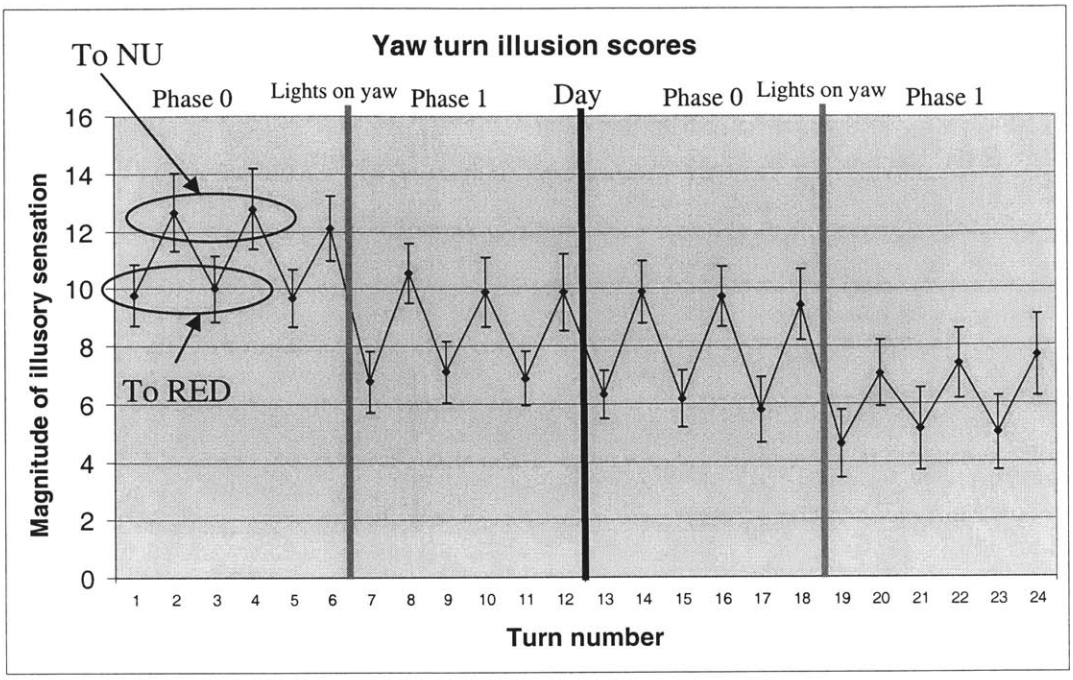


Figure 5.11 Illusion intensity scores for yaw head turns. Note that the first measurement is not an automatic 10 as the first measurements are for pitch, because the yaw movements occur after the first pitch movement that is used as the modulus.

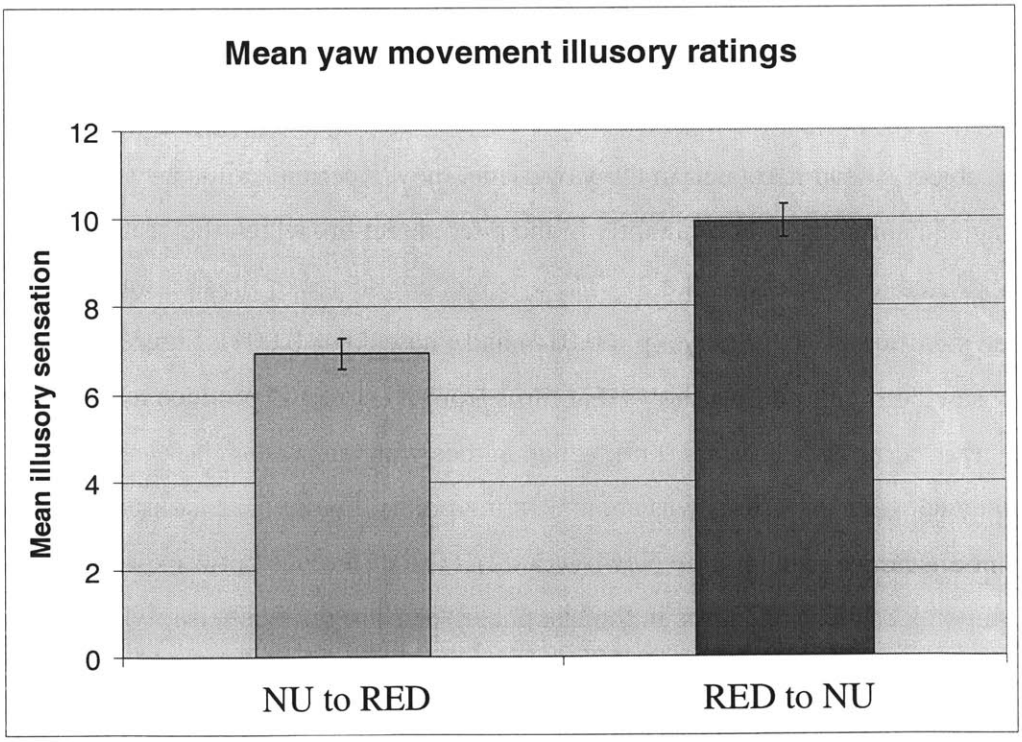


Figure 5.12 Illusory sensations for NU and RED yaw movements. The difference is statistically significant ($p = 0.006$).

5.3.5 – Summary for yaw movements

All of the main adaptation effects were consistent with expectations and past results. At odds with past research is the higher NSPV on turns from NU to RED. However, this pattern does correlate with an illusory intensity trend by Direction observed in this study and by others.

5.4 Pitch head turns

5.4.1 Significant effects

Figure 5.13 shows a typical plot of SPV for the horizontal VOR (HVOR) induced by 6 pitch movements. The noise in all eye data appears to be of equal magnitude, and so the stronger and longer HVOR for pitch movements are generally easier to follow than the weaker vertical VOR signals from yaw turns. Therefore, it is also easier to get better curve fits for the pitch turn SPV plots. A plot of the head turn angles made by all subjects is presented in Figure 5.14. There is some indication that the head pitch-angle increased during the Experimental Group's protocol, while in the Control Group's protocol, the distribution unexpectedly resembles a normal distribution. Table 5.3 presents a summary of the significant ANOVA effects observed for pitch head turns.

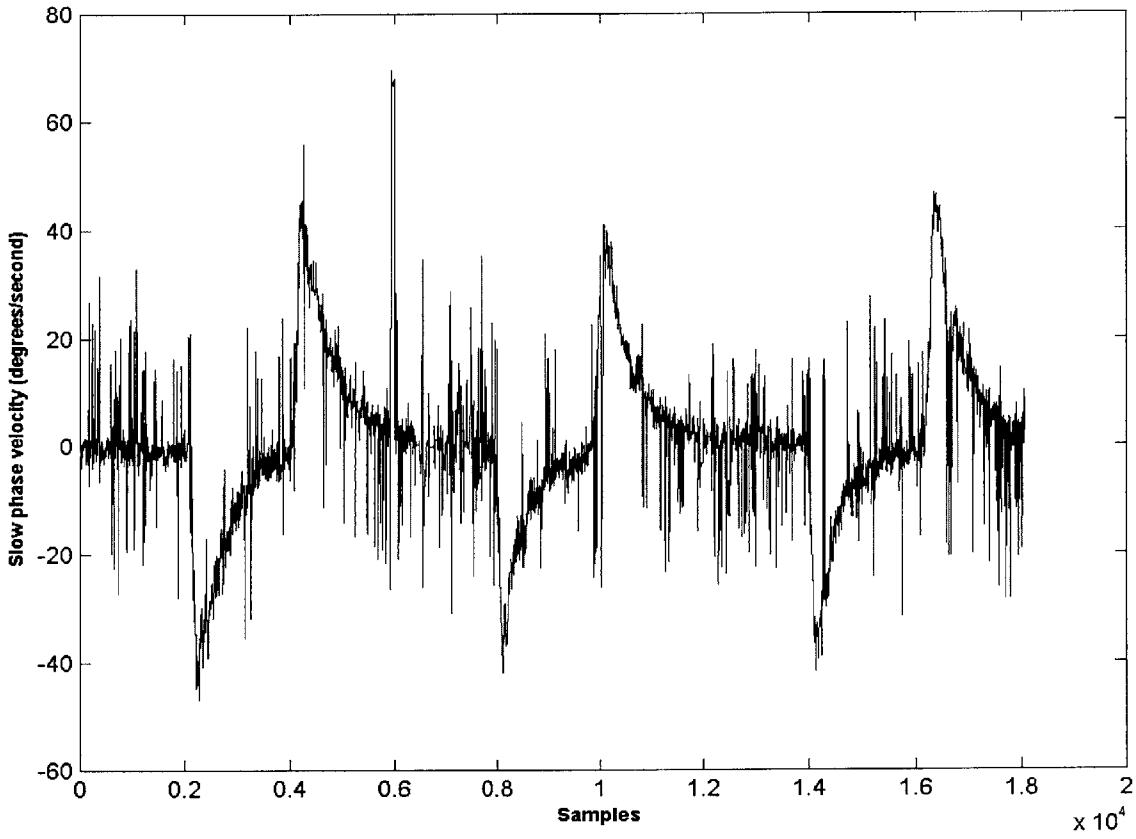


Figure 5.13 Typical block of 6 pitch head turns (Subject 20, first Day, first Phase).

Table 5.3 Table of significant effects at the $p < 0.05$ level. †Denotes approaching significant at $p < 0.06$. N/A = not applicable.

Variable	Day	Phase	Rep	Direction	Cross Group	Other cross effects
Tau	$F(1,16) = 19.750$, $p = 0.0005$	$F(1,16) = 35.669$, $p = 0.0005$	$F(2,32) = 6.472$, $p = 0.007$		Day*Phase*Rep*Direction*Group, ($F(2,32) = 3.609$, $p = 0.039$)	Rep*Direction ($F(2,32) = 5.452$, $p = 0.009$), Day*Phase*Rep ($F(2,32) = 3.899$, $p = 0.031$)
NSPV					Direction ($F(1,16) = 13.054$, $p = 0.002$), Phase*Rep ($F(2,32) = 5.156$, $p = 0.024$), Day*Phase*Direction ($F(1,16) = 4.552$, $p = 0.049$), Day*Rep*Direction ($F(2,32) = 4.321$, $p = 0.022$)	Phase*Rep, ($p = 0.004$, $F(2,32) = 8.396$), Day*Phase*Rep* Gender ($F(2,32) = 3.958$, $p = 0.03$)
Illusion	$F(1,16) = 14.836$, $p = 0.001$				Day*Phase*Rep*Direction*Group, ($F(2,32) = 3.442$, $p = 0.044$)	Phase*Rep ($F(2,32) = 5.725$, $p = 0.007$)
Control						
Tau	$F(1,8) = 9.223$, $p = 0.016$	$F(1,8) = 11.607$, $p = 0.009$,	$F(2,16) = 9.051$, $p = 0.004$,		N/A	Day*Phase ($F(1,8) = 9.365$, $p = 0.016$), Rep*Direction ($F(2,16) = 5.142$, $p = 0.021$)
NSPV					N/A	
Illusion	$F(1,8) = 5.033$, $p^{\dagger} = 0.055$				N/A	Phase*Rep ($F(2,16) = 3.809$, $p = 0.044$)
Exper.						
Tau	$F(1,7) = 6.956$, $p = 0.034$	$F(1,7) = 18.366$, $p = 0.004$	$F(2,14) = 4.414$, $p = 0.033$		N/A	
NSPV				$F(1,7) = 9.289$, $p = 0.019$	N/A	Phase*Rep ($F(2,14) = 7.539$, $p = 0.017$), Day*Phase*Direction ($F(1,7) = 12.985$, $p = 0.009$)
Illusion	$F(1,7) = 5.412$, $p^{\dagger} = 0.053$				N/A	Day*Phase*Direction ($F(1,7) = 5.199$, $p = 0.057$)

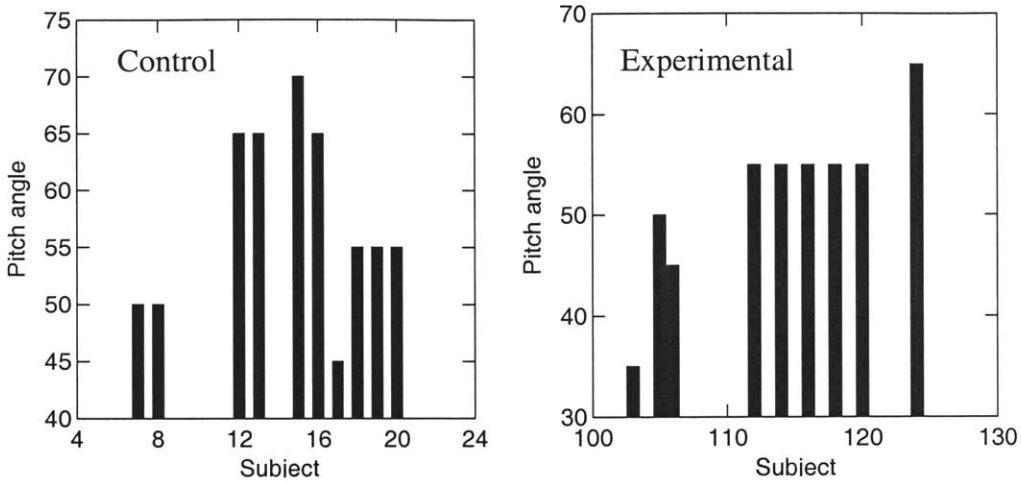


Figure 5.14 Pitch head turn angles in degrees by Group.

5.4.2 HVOR time constant

The complete decay times of HVOR SPV range from about 25-35 seconds, which is not inconsistent with times reported elsewhere (Young and Oman, 1969; Henn, et al., 1980). The length of decay is clearly much longer for HVOR than for vertical VOR from yaw movements. Figure 5.15 shows a histogram of τ values, which is approximately normal, with a mean of 9.0 seconds (Standard Error = 0.16 sec).

Reduction of the HVOR time constant can be seen in Figure 5.16, which plots the values of τ per head turn over Days and Phases. Recall that between turns 6 and 7, and between 18 and 19, the subject performs the entire set of 24 yaw movements. The reductions of τ across Days ($p = 0.0005$) and Phases ($p = 0.007$) are represented in the bar chart in Figure 5.18. No significant main effect in τ was found between Experimental and Control Groups. It may seem from Figure 5.16 that the final 6 turns of the control group dip slightly below the control group. However, when the difference between the two Groups is plotted, it is clear that it falls within the mean standard error of the differences, Figure 5.17. Additionally, the Experimental group will fluctuate slightly above and below the Control Group line with the systematic exclusion of subjects, but always remains quite

similar. The one Group effect was a five-way interaction that is the result of turn 15 being higher than the others, and would not be reasonably linked to the effect of yaw movements.

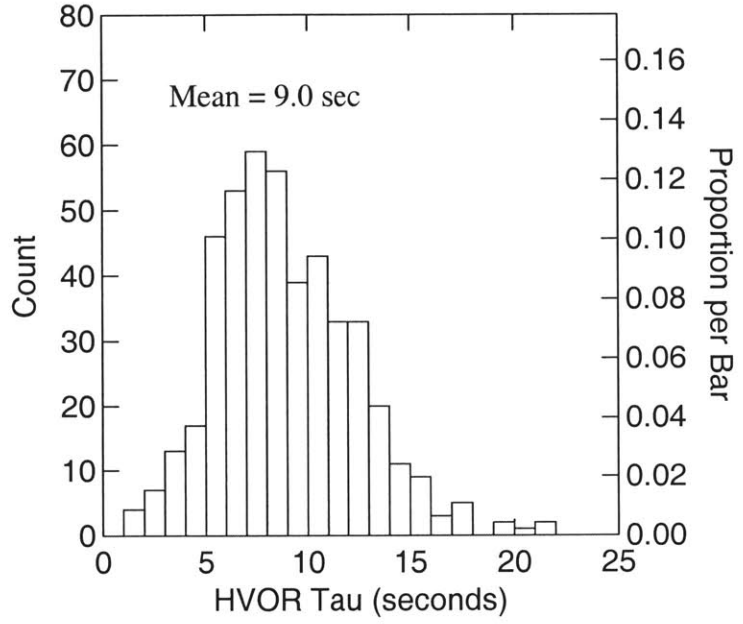


Figure 5.15 Histogram of τ values for the HVOR induced during pitch head movements.

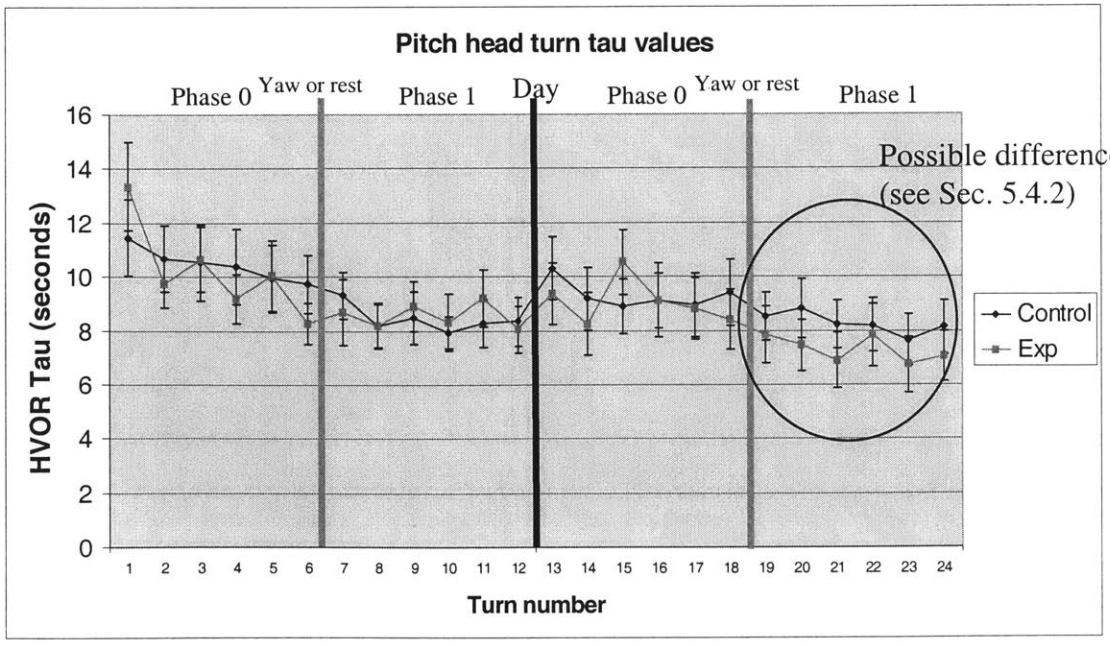


Figure 5.16 HVOR τ values for pitch head turns.

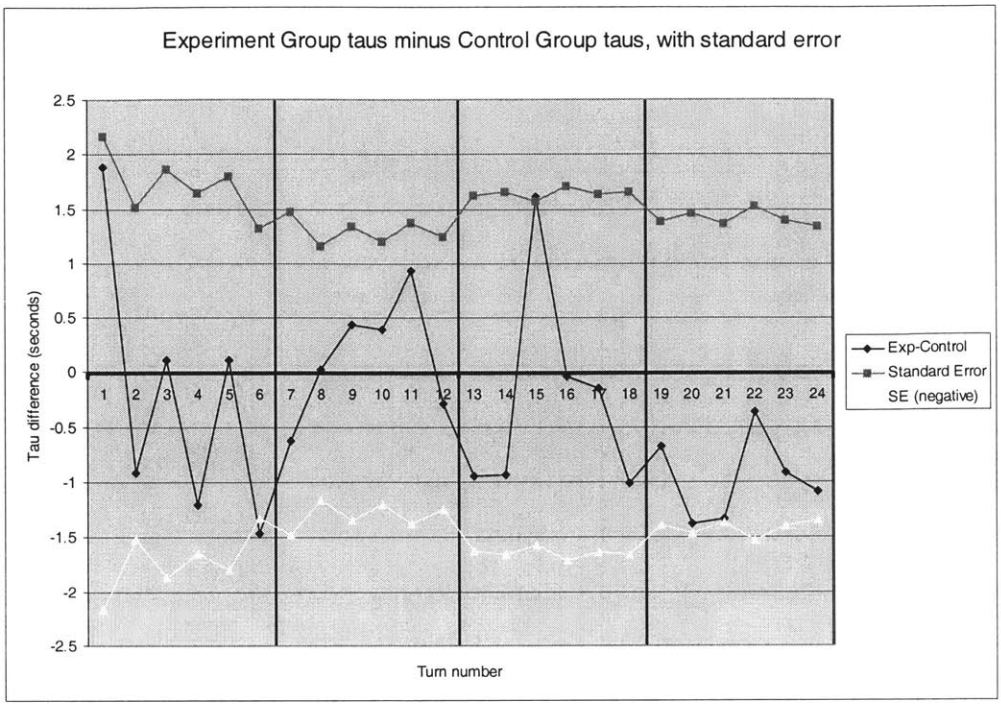


Figure 5.17 Difference in τ values between Experimental and Control Groups. The difference is shown with the limits +/- one standard error.

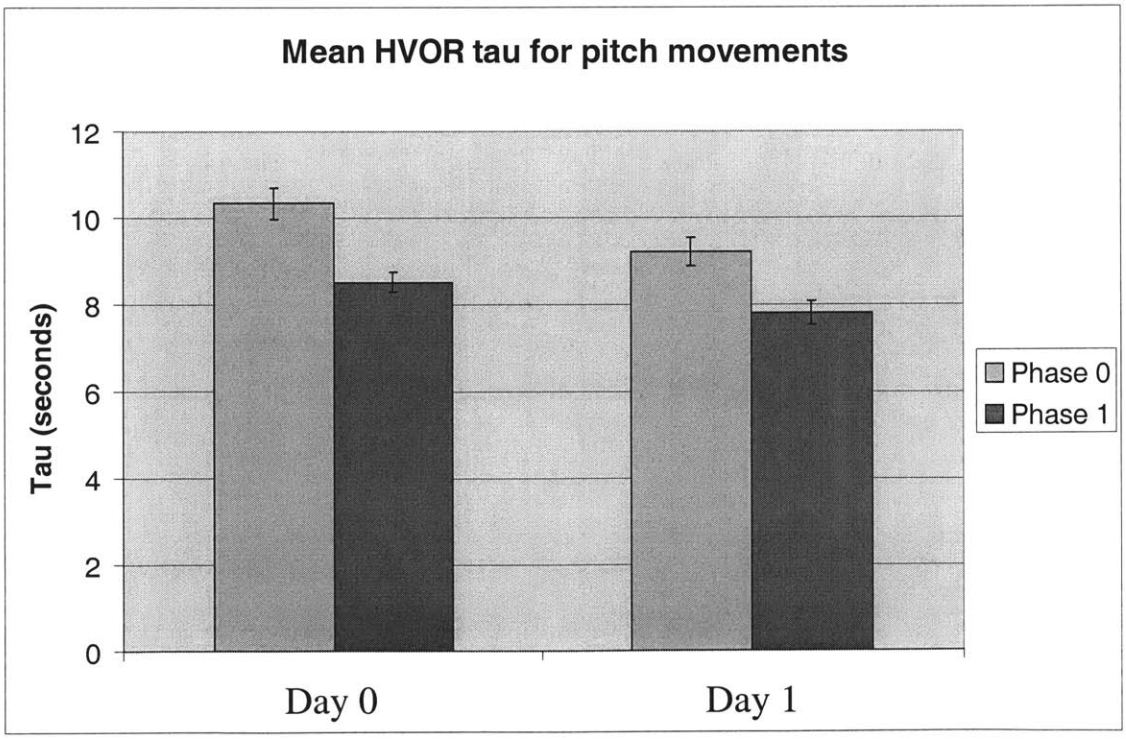


Figure 5.18 Effect of Day and Phase for HVOR τ for pitch head turns (Control and Experimental Groups combined).

5.4.3 Normalized SPV

A histogram of HVOR NSPV values for each Group is shown in Figure 5.19, and the general trend over all 24 head turns is shown in Figure 5.20. A notable feature of the NSPV measurements is that the distribution of the Experimental Group is not normal (it is skewed strongly to the right), but that of the Control is approximately normal. The skewing can also be seen in the generally higher SPV values for each turn (Figure 5.20). While the Experimental Group appears to have higher SPV values, and greater variability, there is no clear increasing or decreasing trend over the experiment. The Control Group is remarkably flat, but also less variable from one head turn to the next. There were no significant main effects of Day or Phase found. The significant effect of Direction in the Control Group is clear from the up and down shifts in Figure 5.20.

The unevenness in the Experimental Group's NSPV values is clearly represented in a box plot of the values for each subject, separated over Days and Phases, Figure 5.21. When compared with a similar plot for the Control Group, Figure 5.22, the Experimental Group's distribution is wider, both within and between subjects. Importantly, the difference in variability is consistent across all Days and Phases, implying that it is not due to the effect of yaw movements.

From the differences in box plots, it is understandable that there are several significant cross-Group effects for NSPV. One interaction that may related to cross adaptation is the Group*Phase*Rep ($p = 0.024$) effect. This effect reflects the following observed difference between the two groups: although the curve of NSPV vs. Repetition is nearly flat for both groups, the Control Group's curve is flatter (Figure 5.23). The Control Group is nearly dead flat for both phases, whereas the Experimental group shows, approximately, a very slightly increasing curve for Phase 0, and a curve that dips slightly in the middle for Phase 1. Neither of the Experimental Group trends by phase is consistent with a pattern of adaptation, and is likely due to the wide variability among

subjects in the Group. The same trend drives the significant Phase*Rep ($p = 0.017$) effect when the Groups are analyzed together.

There are several significant Group effects involving differences in Direction (NU vs. NF). These effects may be due to the yaw movements, or perhaps simply to the large differences observed in the Experimental Group. For example, in Figure 5.24, which plots the Direction difference by Group, there the significant difference between the trends in in each Group. The Control Group shows high NF values and low NU values, while the Experimental Group shows the opposite. However, this trend is apparent even before the yaw turns begin for the Experimental Group (first 6 turns of Figure 5.20), suggesting that the effect grows from inherent traits of the Group itself, and not from the effect of yaw. It may be important that the Experimental Group also showed strong Direction preferences in yaw NSPV that disagreed with the pattern usually observed for yaw NU-RED turns (Section 5.3.3).

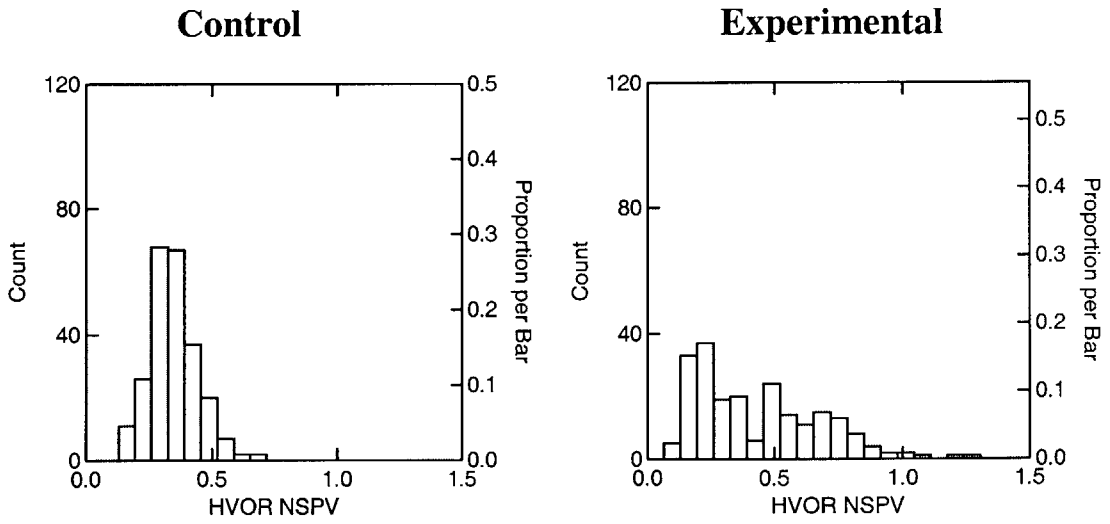


Figure 5.19 Histogram of HVOR NSPV values for the Control and Experimental Group pitch movements.

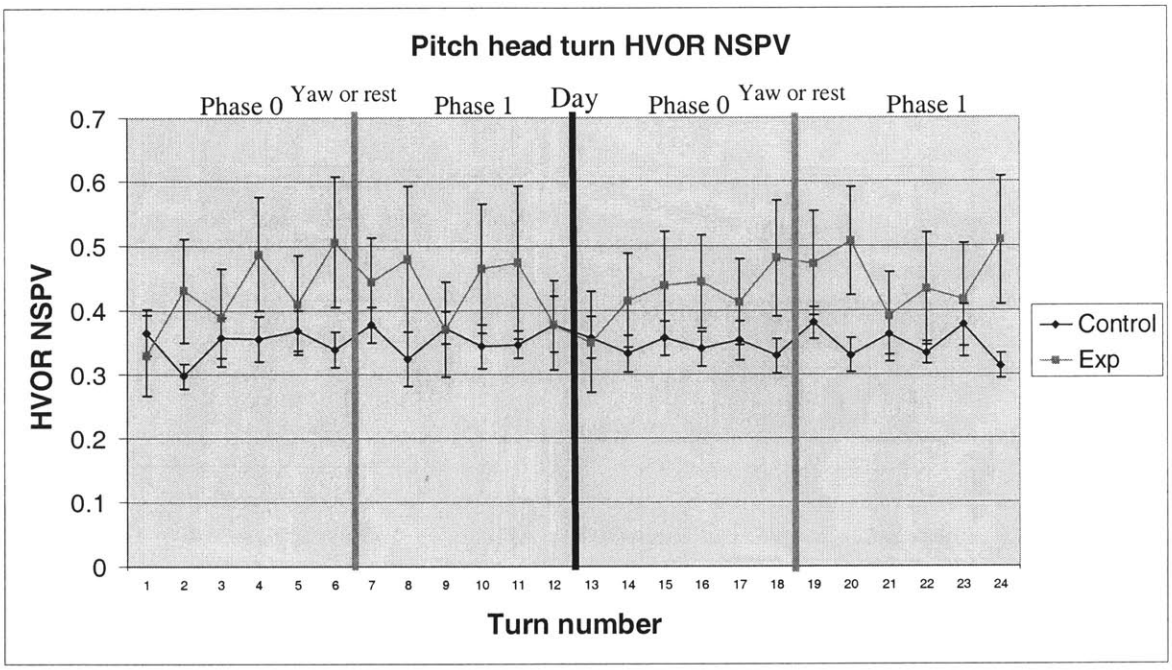


Figure 5.20 HVOR NSPV by turn number for Control and Experimental Groups.

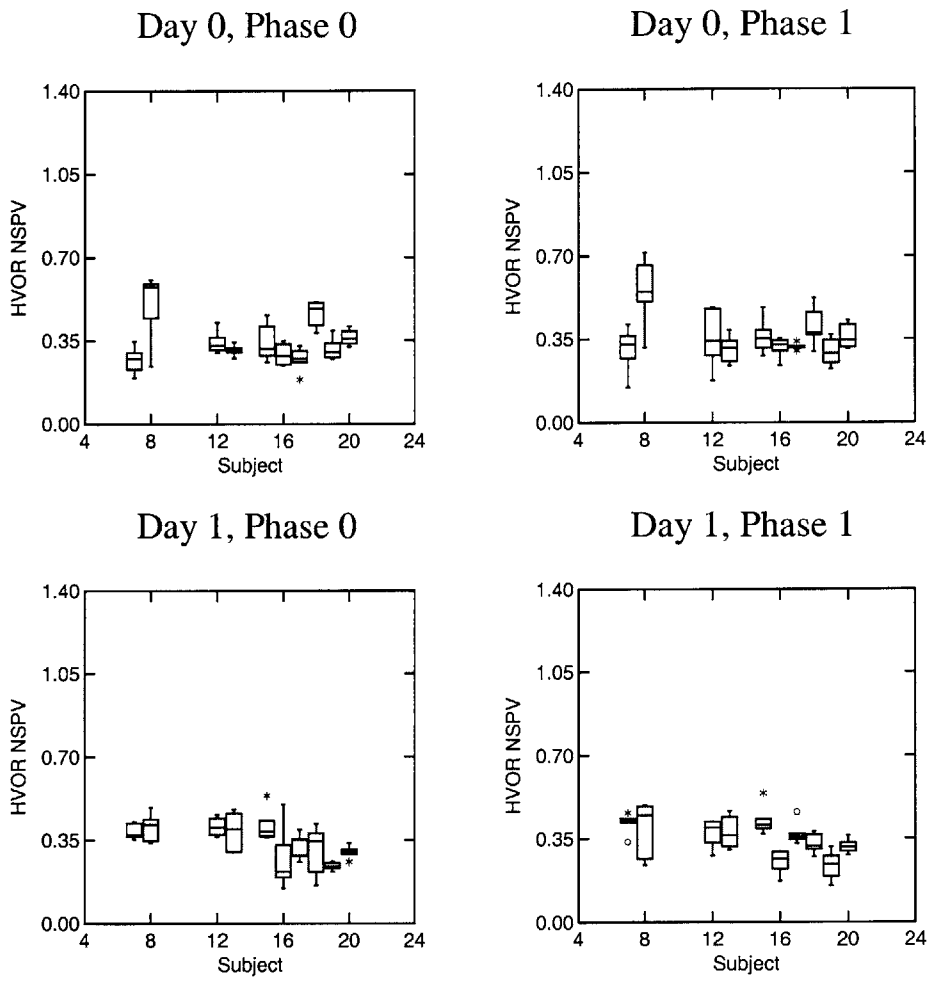


Figure 5.21 Control Group box plots of HVOR NSPV separated by Day and Phase.

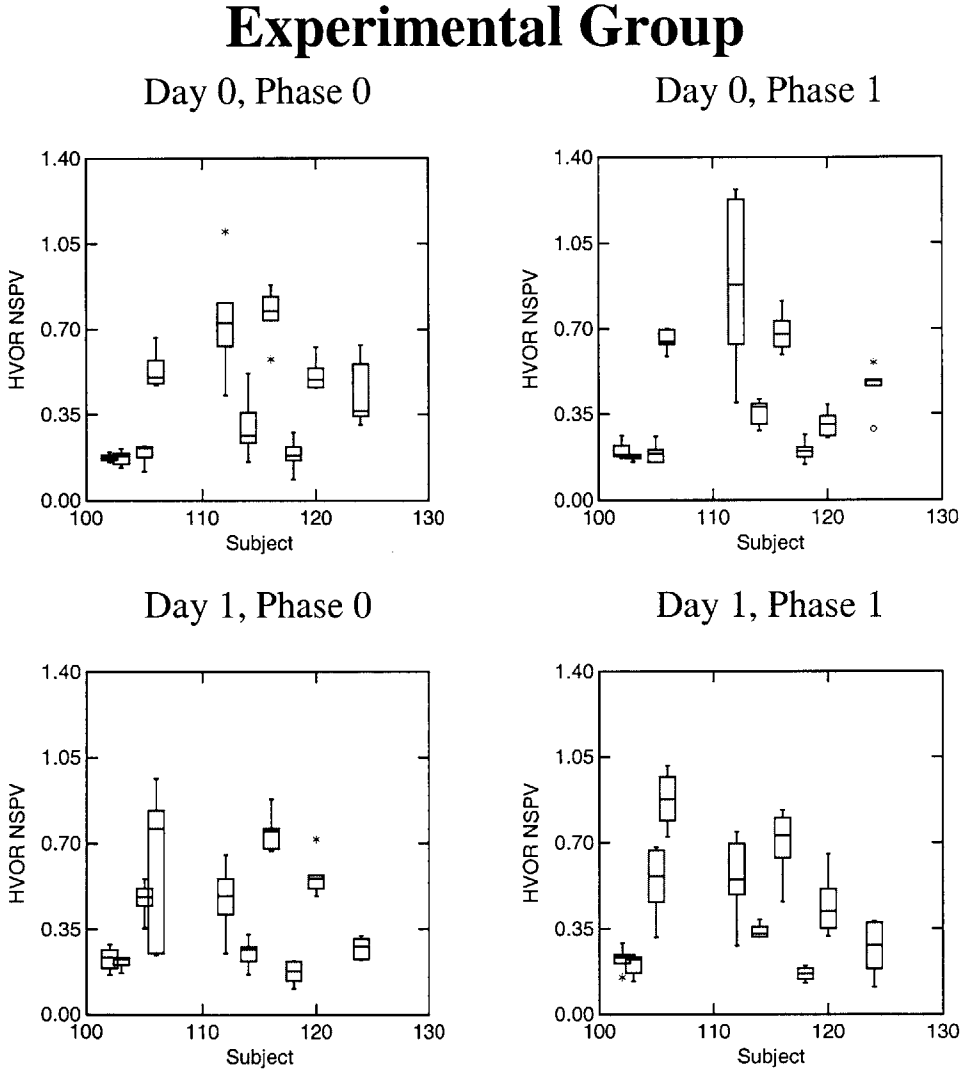


Figure 5.22 Experimental Group box plots of HVOR NSPV separated by Day and Phase. Note the wider dispersion within and between subjects when compared to the Control Group (Figure 5.21), and the generally higher values.

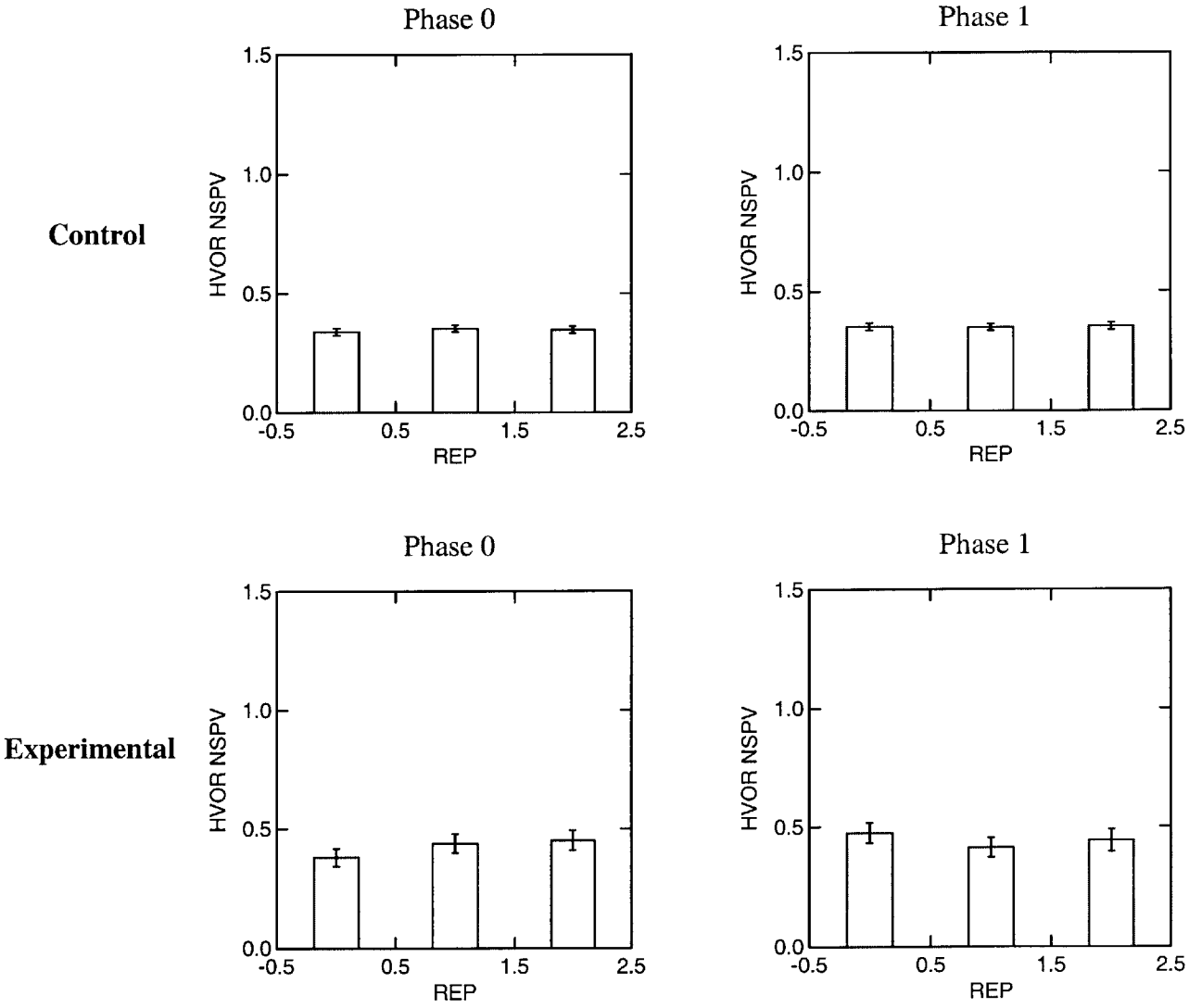


Figure 5.23 Differences between Reps by Phase and Group. The flatness in the Control Group is contrasted by the trends of the Experimental Group, which are probably not the effect of the yaw movements.

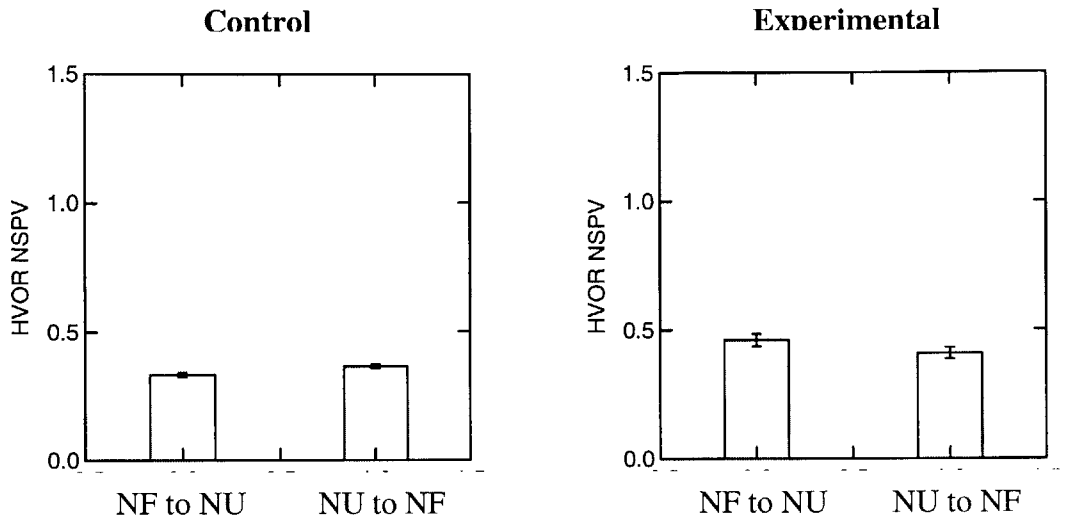


Figure 5.24 Differences between HVOR NSPV values for NU and NF for each Group. The trends for each Group are opposite each other.

5.4.4 Magnitude of illusory sensations

The general decrease in the magnitude of illusory sensation experienced by subjects in both Groups was approximately equal, Figure 5.25, and no main Group effects were observed. The mean score for turns from NU to NF is 9.4 (SE = 0.21), and from NF to NU it is 9.2 (SE = 0.25). The lack of any NF-NU difference contrasts strongly with the difference observed for yaw movements (Figure 5.12).

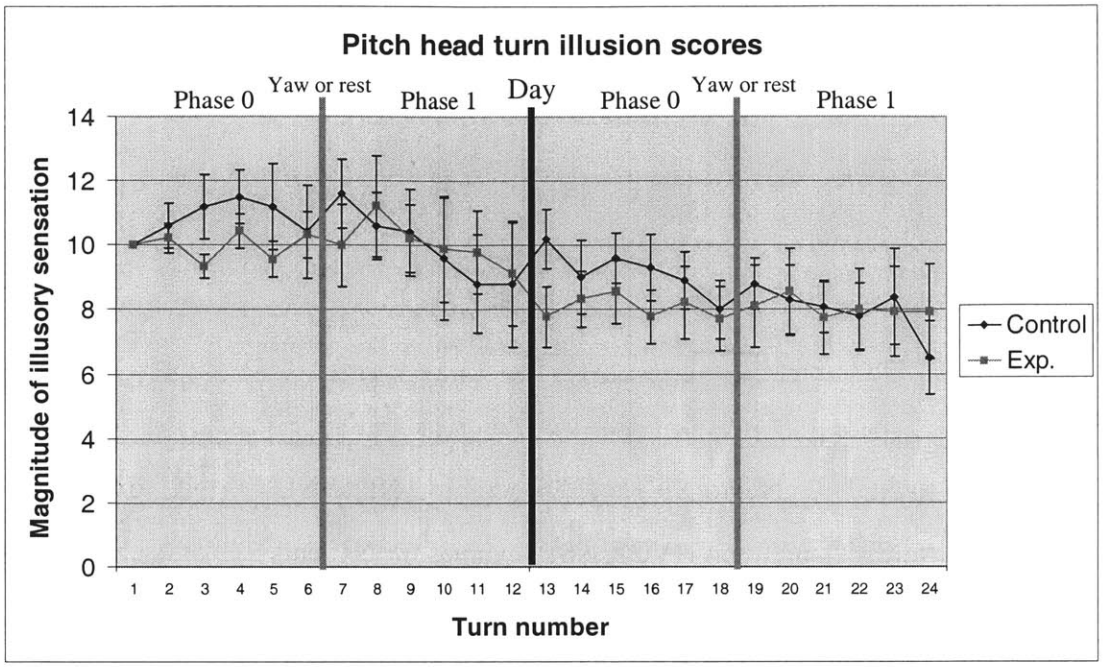


Figure 5.25 Illusory sensation scores per pitch head movement and their standard errors.

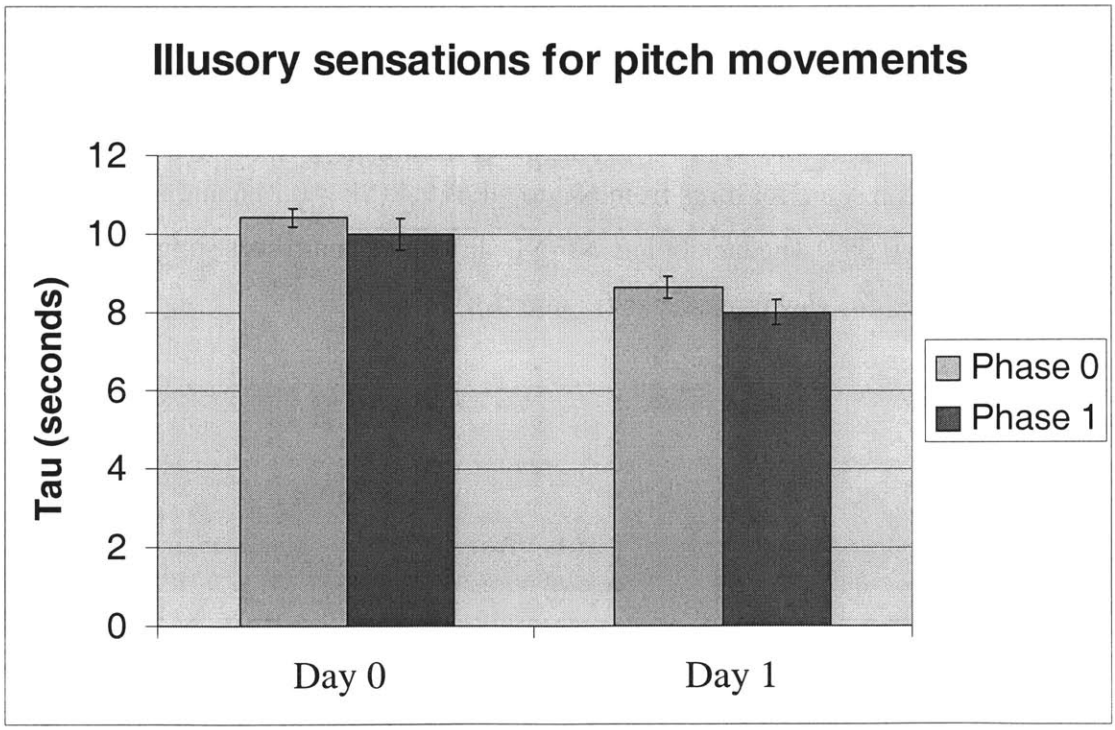


Figure 5.26 Effect of illusory sensation across Phases and Days (aggregated Groups).

5.4.5 Summary for pitch turns

Significant decreases in HVOR τ and NSPV values indicate that adaptation took place. However, no significant main effects of Group were observed that could be linked to the adaptation trends observed in yaw metrics. Large differences between the Groups in NSPV values show no trend that would be expected from an adaptive process.

Chapter 6 - Discussion

6.1 Overview of key findings and explanations

The results of Chapter 5 point to several major findings, which are each discussed in Section 6.2:

1) As observed for yaw head turns in this study and in others, adaptation to pitch head turns is found in the VOR time constant and subjective illusory motion scores. Reduction in the time constant is emphasized here because of its relation to motion sickness.
2) Because the Control Group and Experimental Group showed no significant differences in τ HVOR or illusory sensation, there is no significant transfer of yaw adaptation to adaptation for pitch movements in these metrics.
3) While several cross-Group effects of NSPV were observed, none were main effects of Phase, Day, or Repetition. It is likely that the effects were not due to transfer of adaptation, but rather a fundamental difference between the two groups.

In Section 6.3, two models are presented to explain the lack of transfer:

1) An otolith-canal interaction paradigm for VOR adaptation that suggests different otolith cues received during different head turns constitute unique stimuli that are handled separately. This model suggests information is processed in otolith coordinates.

2) A neurophysiological model that localizes velocity storage and VOR adaptation for each axis in distinct zones of the nodulus of the vestibulocerebellum. This model suggests information is processed in canal coordinates.

Section 6.4 discusses implications of the findings for adaptation to SRC, and Section 6.5 contains recommendations on adaptation protocols, future research directions, and experimental modifications.

6.2 Adaptation and lack of transfer

6.2.1 Adaptation to pitch head turns

At the most basic level it is promising that subjects showed adaptation to pitch head turns. The horizontal VOR time constant and illusory motion scores drop by both Phase and Day over the course of the experiment. It is interesting to note that the decrease is quite visible over a small number of head turns, 24, when compared to the number of yaw turns performed in other experiments that have had over 60 head turns (Sienko, 2000; Brown, 2002). It may be that the pitch head movements show a greater decrement than the yaw turns over the same number of trials, or that both groups decline similarly and reach a plateau. If a plateau is reached, it would make sense to stop at this point and continue the next day, implying an emphasis on days of adaptation, rather than longer single day sessions.

The importance of time constants as a metric for adaptation is emphasized in this study, in contrast to other studies where reductions in NSPV were emphasized (Siekno, 2000; Brown, 2002). This metric is chosen because it is most likely linked to the generation of motion sickness, and evidence of its reduction over days could be linked to reduced motion sickness. Additionally, the time constant can be adapted without cues from a visual field. Therefore, understanding how the time constant changes probably reveals more information about the vestibular system's internal model of motion.

Overall, the NSPV values do not rise or fall over both days, but we do not expect any change since the pitch head turns were conducted in darkness, affording no opportunity for incorrect horizontal retinal slip to occur. There was no difference found between

illusory intensity for NU and NF turns, which contrasts the directional difference observed for yaw turns. Accordingly, there was no correlation between NU and NF, with either of the two VOR metrics.

6.2.2 Lack of transfer

Our failure to find any transfer between the two planes is most visible in the time constant and illusory motion metrics. Both the Control Group and Experimental Group trends decrease over Phases and Days quite similarly, and there are no statistically significant main cross-Group differences. While it is impossible to prove a negative result, it appears that on the timescale this experiment was conducted, it does not matter if the subject performs pitch turns and yaw turns together or separately. However, it is worthwhile pointing out that in pitch turn numbers 19-24, the time constant values for the Experimental Group are consistently lower than they are for Control Group (Figure 4.16).

For the two five-way interactions of Day*Phase*Rep*Direction*Group observed for illusion scores and time constants, these can be explained by deviations of only one head turn out of 24. Since the significance level being used is one out of twenty ($p = 0.05$), it is not unlikely one of the 24 head turns is statistically different from one of the turns in the other Group.

6.2.3 VOR NSPV results show Group differences

The NSPV values for the Control Group are remarkably flat, and show no trend over all Phases and Days. However, the Experimental Group's higher and more variable NSPV values produce several cross-Group effects that are worth mentioning. When analyzed alone, the Experimental Group shows a significant effect of Direction, and it is the lack of an effect of Direction in the Control Group that makes the cross-effect statistically significant. All other cross-Group Direction effects stem from this difference, but they are not indicative of a general trend toward decreasing values over time, since the Direction factor is only an alternating measurement. Most importantly, there are no main

cross-Group effects of Day, Phase, or Repetition, which are all factors that involves changes over time (adaptation). Additionally, while the NSPV values of the Experimental Group are variable, there is no visual trend towards decreasing values. The Experimental Group starts high, and ends high. Based on these findings, there is likely no effect of yaw turns on the Experimental Group, insofar as what would be expected if there were transfer of adaptation.

6.3 Explanations for the apparent lack of transfer

6.3.1 Otolith-canal interaction

Considerable work has showed that VOR is dependent on the gravito-inertial context. As described in the background chapter, the phenomenon of dumping is a good example of how VOR can be changed by a different gravity cue. When tilt dumping of post-rotatory nystagmus is performed in weightlessness, the VOR time constant is not reduced as much as it is on the ground because of the missing gravity cue (Oman and Balkwill, 1993). More recent work has focused on the gravito-inertial force (GIF) resolution hypothesis. In the GIF resolution paradigm, the central nervous system (CNS) estimates the difference between the actual GIF and the perceived GIF. The CNS uses both the semicircular canals and the otolith organs to make its estimate. Zupan and others (2000) found that the GIF hypothesis accurately predicted the direction of post-rotatory nystagmus in two rotation protocols, confirming the interaction of the otolith cues in orienting VOR.

If otolith information is essential in estimating VOR, then it could be that the different gravity cues encountered during yaw turns and pitch turns cause each stimulus to be treated separately. A head turn that changes the gravity vector from moving perpendicular to the body's coronal plane (NU) to through the transverse axis (NF), and vice versa, could be significantly different from turns from the coronal to sagittal plane (RED).

This otolith-coordinate paradigm for determining the appropriate VOR response is also in agreement with Tiliket et al. (1993), who found no transfer of VOR gain from a vertical rotating chair training position to a head tilted position (Section 2.7). The lack of transfer observed in Tiliket supports the failure to find transfer in this study.

6.3.2 Neurophysiology

Several studies have shown that removal of the nodulus in animals can affect the ability of the central time constant to shorten after repetitive stimuli (Waespe et al, 1985; Cohen et al., 1992). The actual velocity storage mechanism may be located in the vestibular nucleus, which receives afferent signals from vestibular organs and controls the motion of the eye (Cohen et al., 1999). However, the nodulus plays a role in mediating the time constant after central processing of the estimates of motion have been performed in canal-coordinates (Cohen et al., 1999). The nodulus has direct nerve projections to the vestibular nucleus that accomplish this regulation, as observed in rabbits and extrapolated to rhesus monkeys (Barmack et al., 2002; Walberg and Dietrichs, 1988). These nerve projections are also associated with separate "sensitivity axes", where rotation of the head in each plane causes preferential firing activity in that projection (Wearne, et al., 1998).

The more specific role of the nodulus in regulating the three-dimensional spatial orientation of the VOR response has also been studied in rabbits (Barmack et al., 2002). According to a summary by Wearne et al. (1998), work by Angelaki and Hess (1994a, 1994b) determined that monkeys maintained reductions in torsional VOR time constants after partial nodulectemy, but lost adaptability in vertical VOR. These findings imply that the separate parts of the nodulus are responsible for at least two different axes of motion. Additionally, preliminary results of Wearne et al. (1996) showed that distinct portions of the nodulus were responsible for regulation in all three axes. Wearne et al. (1998) showed that lateral nodulectomy affected horizontal VOR velocity storage, and central nodulectomy affected roll and torsional VOR, as discussed in Section 2.3.4. In all, there is believed to be complete zonation of the nodulus for each rotation axis in the rhesus monkey (Wearne, 2004).

All of the above studies indicate that each of the three axes of the semicircular canals may be treated separately with regard to regulation of the VOR time constant. This implies that there is a distinct canal-coordinate frame calculation of motion for turns within each plane of motion. Under this model, each axis would have to be adapted separately.

It is likely that the true model for estimating the VOR time constant and other VOR parameters results from a combination of the otolith and canal-coordinate systems.

6.4 Implications

The lack of transfer between planes suggests that SRC users will probably have to adapt to each axis of head motion separately. This forces a tradeoff between spending many days on the centrifuge adapting one plane at a time, or spending fewer days performing head turns in both planes with a greater likelihood of becoming sick. The results of incremental adaptation studies may also factor in to how this tradeoff should be decided.

An important question that arises is if once adaptation to the three principle axes is established, will it transfer to any arbitrary plane (e.g. a diagonal head movement)? If the otolith-canal interaction model is correct, then diagonal head turns would still be provocative, since they would involve a different gravity cue. However, some generalization might be expected. If the canal-coordinate system is correct, then a diagonal turn would probably not be provocative. In this case all canals would be stimulated at once, and each should be in an adaptive state unless there are significant interaction effects between them. Even if there were interaction between all three canals, some generalizations would again be expected due to the similarity of the stimuli.

Transfer of adaptation across planes might be possible in microgravity if the otolith-canal interaction explanation is responsible for the lack of transfer. In microgravity there would be no otolith cue to differentiate turn positions in each axis. However, if the

influence of otolith cues is strong enough, then any adaptation gained on Earth might not transfer to adaptation on orbit. If the canal-coordinate model is responsible for lack of transfer, then adaptation for separate axes would still be required in microgravity.

If it is found that living on the Moon or Mars does not provide sufficient gravity to prevent deleterious health effects, then AG used in these environments would be subject to the same transfer adaptation rules as on Earth, although with possibly less dependence on gravity. In the otolith-coordinate system model though, the new gravity environment could preclude transfer of any adaptation gained on orbit, or possibly even on Earth.

6.5 Recommendations and future work

1) Again, while it is impossible prove a negative result, the current experiment could be refined to understand how much or how little adaptation transfers between planes. By performing the protocol over more than two days, the τ value trend for pitch turns in Figure 2.16 could be followed to see if the two Groups diverge significantly. Additionally, performing more yaw turns within a day could help establish a greater adaptation response to yaw, which could show up stronger in the pitch head turns. The number of yaw turns, however, would always be constrained by motion sickness.

2) If it found that that transfer likely does not take place, it would probably be worthwhile to study if the otolith-coordinate or canal-coordinate paradigm is responsible. A more involved experiment using parabolic flight could resolve the two theories using a rotating chair with roll and pitch head turns. If cross-axis adaptation is found in microgravity, then it would imply an otolith-coordinate frame.

3) Determine if discomfort within a day, or the number of days spent spinning is the limiting factor when designing a general adaptation protocol for all planes. Performing all turns on one day will make the subject sick, but lengthening the protocol over many days may be too time consuming, and increase the total time the subject is ill. Results from studies on incremental adaptation should be incorporated.

4) Find the end point where adaptation typically stops within a day, if it exists, and terminate the daily session at that point.

5) Future studies on the topic of transfer should be aware of a possible increase of NSPV in the group that receives the treatment head turns, since that variable showed the most variability this experiment.

6) Consider using pitch turns instead of yaw turns for any future adaptation studies, since less is known about these movements, and SPV curve fits are obtained much more easily.

7) Refine the head stopping mechanism for pitch movements and fix the angle of head movement for all subjects and planes to make more similar comparisons. Almost all subjects were able to pitch forward over 50 degrees, which was more than enough to elicit a strong VOR response. Normalizing by angle of head turn seems to only complicate the measurements.

Chapter 7 - Conclusions

While the statistical tests used in this experiment showed no significant main-effect differences between the Control Group's adaptation to pitch movements, and the Experimental Group's adaptation, the problem of proving a negative result leaves open the possibility that transfer might occur. It is possible that more sensitive experiment designs could detect some difference and show that the brain builds up a generalized model for cross-coup'ed vestibular stimuli. Performing these experiments is probably worth doing, but the guiding question should be how much transfer of adaptation is needed to be of practical use in adapting subjects? If it turns out that a small amount of transfer takes place over several days, perhaps evidenced through a 0.5 second difference in mean VOR time constants, then it still may not be worth performing yaw and pitch movements together. Additionally, if future experiments find that there is no difference between the Groups to within a 0.5 second difference, then it may not make sense to continue looking for an effect. What constitutes a practical amount of transfer, and how that transfer should be measured, still remains an open question.

References

Angelaki, D.E. and Hess, B.J.M. (1994a) The cerebellar nodulus and ventral uvula control the torsional vestibulo-ocular reflex. J. Neurophysiol. 72: 1443–1447

Angelaki, D.E. and Hess, B.J.M. (1994b) Inertial representation of angular motion in the vestibular system of rhesus monkeys. I. Vestibuloocular reflex. J. Neurophysiol. 71: 1222–1249

Balkwill, M.D. (1992) Changes in human horizontal angular VOR after the Spacelab SLS-1 mission. Unpublished S.M. Thesis, Massachusetts Institute of Technology.

Barmack, N. H., et al. (2002) Cerebellar nodulectomy impairs spatial memory of vestibular and optokinetic stimulation in rabbits, Journal of Neurophysiology 87, 632-975.

Berry, C. A. (1970) Summary of Medical Experience in the Apollo 7 Through 11 Manned Space Flights, Aerospace Medicine 41, 500-519.

Bockisch, C. J., Straumann, D., and Haslwanter, T. (2003), Eye movements during multi-axis whole-body rotations, Journal of Neurophysiology 89, 355-266.

Bos, J. E., Bles, W., Graaf B de (2002) Eye movements to yaw, pitch, and roll about vertical and horizontal axes: adaptation and motion sickness. Aviation Space and Environmental Medicine 73, 436-434.

Brown, E. L. (2002) Artificial gravity: The role of visual inputs in adaptation to short-radius centrifugation. Unpublished SM Thesis, Massachusetts Institute of Technology.

Brown, E. L., et al. (2003) Sensorimotor aspects of high-speed artificial gravity: I. Sensory conflict in vestibular adaptation, Journal of Vestibular Research, p. 271-282.

Caiozzo, V. J., et al. (2004) Hemodynamic and metabolic responses to hypergravity on a human-powered centrifuge, Aviation, Space, and Environmental Medicine 75 (2), 101-108.

Cohen, B., Matsuo, V., and Raphan, T. (1987) Baclofen and velocity storage: a model of the of the effects of drug on the vestibulo-ocular reflex in the rhesus monkey, Journal of Physiology (London) 293, 703-725.

Cohen, H., Cohen, B., Raphan, T., and Waespe, W. (1992) Habituation and adaptation of the vesitbuloocular reflex: a model of differential control by the vestibulocerebellum, Experimental Brain Research 90, 526-538.

Cohen B., Wearne S., Dai M., Raphan T. (1999) Spatial orientation of the angular vestibulo-ocular reflex. J. Vestib. Res. 9(3), 163-72.

Cohen, B., et al. (2002) The nodulus and uvula: source of cerebellar control of the spatial orientation of the angular vestibulo-ocular reflex, Annals of the NY Academy of Science 978, 28-45.

Cohen, B., Dai, M., and Raphan, T. (2003) The critical role of velocity storage in production of motion sickness, Annals of the New York Academy of Science 1004, 359-376.

Cramer, D. B., Graybiel, A., and Oosterveld, W. J. (1978) Successful transfer of adaptation acquired in a slow rotation room to motion environments in Navy flight training, Acta Otolaryngol 85, 74-84.

Dai, M., Klein, A., Cohen, B., and Raphan, T. (1999) Model-based study of the human copular time constant, Journal of Vestibular Research 9, 293-301.

Dai, M., Kunin, M., and Raphan, T. (2003) The relation of motion sickness to the spatial-temporal properties of velocity storage, Experimental Brain Research 151, 173-189.

Diamandis, P. H. (1988), The artificial gravity sleeper: a deconditioning countermeasure for long duration space habitation. Unpublished S.M. Thesis, Massachusetts Institute of Technology.

DiZio, P., and Lackner J.R. (1991) Motion sickness susceptibility in parabolic flight and velocity storage activity, Aviation Space and Environmental Medicine 62, 300-307.

DiZio P., Lackner J.R. (1992) Influence of gravitoinertial force level on vestibular and visual velocity storage in yaw and pitch: Vision Res. 32(1), 111-20.

Edgerton V.R. and Roy R. R. (1996) Neuromuscular adaptations to actual and simulated spaceflight. In: Handbook of Physiology. Environmental Physiology. Bethesda, MD: Am. Physiol. Soc., Ssect.4, vol.II, chapt 32,.721–763.

Fitts, R.H., Riley, D.R., Widrick, J.J. (2000) Physiology of a microgravity environment invited review: Microgravity and skeletal muscle. J Appl Physiol 89:823–39.

Graybiel, A., Miller E.F., and Homick, J.L. (1977), Experiment M131, Human vestibular function, in *Biomedical results from Skylab*, R.S. Johnston and L.F. Dietlein, eds, NASA: Washington, pp. 74-103.

GRIN (1968) Great Images in NASA: http://grin.hq.nasa.gov, accessed May 2004.

Guedry, F. E., Collins, W. E., and Graybiel A. (1964), Vestibular habituation during repetitive complex stimulation: a study of transfer effects, Journal of Applied Physiology 19, 1005-1115.

Guedry, F. E. (1964) Visual control of habituation to complex vestibular stimulation in man, Acta-Otolaryngology, 58, 377-389.

Guedry, F. E. (1965) Habituation to complex vestibular stimulation in man: transfer and retention of effects from twelve days of rotation at 10 rpm, Perceptual and Motor Skills 21, 459-481 (Monograph Supplement 1-V21).

Hacker, B.C. (1977) *On the Shoulders of Titans: A History of Project Gemini*, Published as NASA Special Publication-4203 in the NASA History Series.

Hecht, H., et al., (2002) Adapting to artificial gravity (AG) at high rotational speeds. Journal of Gravitational Physiology 9, P1-P5.

Henn, V., Cohen, B. & Young, L.R (1980). "Visual-vestibular interaction in motion per ception and the generation of nystagmus," Neurosciences Research Program Bulletin (NRP) 18(4).

Homick J.L. (1979) Space motion sickness, Acta Astronautica 6, 1259-72.

Iwase, S., et al. (2003) Effects of simultaneous load of centrifuge-induced artificial gravity and ergometer exercise as the countermeasures for space deconditioning on human cardiovascular function, Journal of Gravitational Physiology 10(1), P101-104.

JSC (2004), Johnson Space Center Image Archive, http://images.jsc.nasa.gov, accessed May 2004.

Kanas, N., Salnitskiy, V., Grund, E., Gushin, V., Weiss, D.S., Kozerenko, O., Sled A., and Marmar, C.R. (2002) Lessons learned from Shuttle/Mir: psychosocial countermeasures, Aviation, Space and Environmental Medicine 73, 607-11

Lackner, J. R., & Graybiel, A. (1984). Elicitation of motion sickness by head movements in the microgravity phase of parabolic flight maneuvers. Aviation, Space, and Environmental Medicine, 55, 513-520.

Larson, W. J., and Pranke, L. K. (1999) *Human Spaceflight: Mission Analysis and Design*, McGraw-Hill Primis Custom Publishing.

Maklad, A., and Fritzsch, B. (2003) Partial segregation of posterior crista and saccular fibers to the nodulus and uvula of the cerebellum in mice, and its development, Brain Res. Dev. Brain Res., 140,223-236.

MIT (2004), Space biomedical and life support engineering course website: http://paperairplane.mit.edu/16.423J, accessed May 2004.

NASA (2003), Human Spaceflight Gallery: http://spaceflight.nasa.gov, accessed May 2004.

Newby, N. J., (2002) Artificial Gravity: The role of graviceptive information during cross-coupled rotation in context-specific adaptation. Unpublished SM Thesis, Massachusetts Institute of Technology.

Ohnishi, T., Takahashi, A., Ohnishi, K. (2001) Biological effects of space radiation, Biol. Sci. Space, 15 Supplement: S203-10.

Oman, C. M., and Balkwill, M. D. (1993). Horizontal angular VOR, nystagmus dumping, and sensation duration in Spacelab SLS-1 crewmembers. Journal of Vestibular Research, 3, 315-330.

Paloski, W. H., et al. (2003) Pilot Study of Artificial Gravity as a Multi-System Countermeasure to Bed Rest Deconditioning, Project Proposal submitted to NASA.

Parker J. F., and West, V. R. (1973) Bioastronautics Data Book, Second edition, NASA SP-3006.

Raphan, T., Matsuo, V., and Cohen, B. (1979) Velocity storage in the vestibulo-ocular reflex arc (VOR). Exp Brain Res 35:229–248.

Reason, J. T. (1975) *Motion Sicknes*, Academic Press, New York.

Schneider SM, Amonette WE, Blazine K, Bentley J, Lee SM, Loehr JA, Moore AD Jr, Rapley M, Mulder ER, and Smith SM. (2003) Training with the International Space Station interim resistive exercise device, Med Sci Sports Exerc. 35, 1935-45.

Sheliga, B. M, et al. (1999) Control of spatial orientation of the angular vestibulo-ocular reflex by the nodulus and uvula of the vestibulocerebellum, Annals of the N Y Academy of Science, 871, 94-122.

Shipov, A. A., Kotovskaya, A. R., and Galle, R. R., (1981), Biomedical aspects of artificial gravity, Acta Astronautica, 8 (9-10), 1117-1121.

Sienko, K. (2000) Artificial gravity: adaptation of the vesibulo-ocular reflex to head movements during short-radius centrifugation, Unpublished MIT Master's thesis.

Singleton, GT (1967) Relationships of the cerebellar nodulus to vestibular function: a study of the effects of nodulectomy on habituation. Laryngoscope 77, 1579–1619.

Sonnenfeld G, and Shearer WT (2003) Immune function during space flight, Nutrition 18, 899-903.

Tiliket, C., et al., (1993) Adaptation of the vestibulo-ocular reflex with the head in different orientations and positions relative to the axis of body rotation, Journal of Vestibular Research 3, 181-195.

Turner, R.H. (2000) Invited review: What do we know about the effects of microgravity on bone? Journal of Applied Physiology 89, 840 –7.

VEDA (2004), Vestibular Disorder Association website, http://www.vestibular.org, accessed May 2004.

Vernikos J. (1997) Artificial gravity: intermittent centrifugation as a space flight countermeasure. J Gravit Physiol 4: P13–P16.

Vernikos J., Ludwig D.A., Ertl A., Wade C.E., Keil L., and O'Hara D.B. (1996). Effect of standing or walking on physiological changes induced by head down bed rest: implications for space flight. Aviat. Space Environ. Med 67, 1069–1079.

Walberg F. and Dietrichs E. (1988) The interconnection between the vestibular nuclei and the nodulus: a study of reciprocity. Brain Research 449, 47–53.

Waespe W., Cohen, B., and Raphan, T. (1985) Dynamic modification of the vestibulo-ocular reflex by the nodulus and uvula. Science 228, 199–202.

Wearne, S., Raphan, T., and Cohen, B. (1998) Control of Spatial Orientation of the Angular Vestibuloocular Reflex by the Nodulus and Uvula, Journal of Neurophysiology 79, 2690-2715

Wearne, S., Cohen, B., and Raphan, T. (1996) Nodulo-uvular control of central vestibular dynamics determines spatial orientation of the angular vestibuloocular reflex. Ann. NY Acad. Sci. 781: 364–384.

Wearne, S. (2004) Personal communication.

Welch R. B., et al. (1998), Dual adaptation and adaptive generalization of the human vestibulo-ocular reflex, Perception and Psychophysics 60(8), 1415-1425.

Welch, R. B., (1978) *Perceptual Modification, Adapting to Altered Sensory Environments*, Academic Press, New York.

Wilson, V.J. and Melvill-Jones, G. (1979), *Mammalian Vestibular Physiology*, Plenum Press, New York.

Von Braun, W. and Ordway, F. I, III (1975) *History of Rocketry and Space Travel* III, p. 202.

Young, L. R. (1999), Artificial Gravity considerations for a mars exploration mission, Annals of the New York Academy of Science, 871, 367-378.

Young, L.R. and Oman, C.M. (1969) "Model for vestibular adaptation to horizontal rotation," Aerospace Medicine 40 (10): 1076-1080.

Young, L. R., Hecht H., Lyne, L. E., Sienko, K. H, Cheung, C. C. and Kavelaars, J. (2001) Artificial gravity: head movements during short radius centrifugation. Acta Astronautica 49, 215-26.

Young, L. R., et al. (2003), "Neurovestibular aspects of short-radius artificial gravity: towards a comprehensive countermeasure", Project proposal to the National Space Biomedical Research Institute, July 2003.

Young, L. R. (2003) "Artificial Gravity." Encyclopedia of Space Science and Technology. New York: John Wiley & Sons, Inc., publication, volume 1, pp. 138-151.

Zange J., Muller K., Schuber M., Wackerhage H., Hoffmann U., Gunther R.W., Adam G., Neuerburg J. M., Sinitsyn V. E., Bacharev A. O, and Belichenko O. I. (1997) Changes in calf muscle performance, energy metabolism, and muscle volume caused by Long term stay on space station MIR. Int J Sports Med 18: S308–S309.

Zhang, L.F., Mao, Q.W., Ma, J., and Yu Z.B. (1996) Effects of simulated weightlessness on arterial vasculature—an experimental study on vascular deconditioning. J Gravit Physiol 3, 5–8.

Zhang, L.F., Yu, Z.B., Ma, J., and Mao, Q.W. (2001) Peripheral effector mechanism hypothesis of post flight cardiovascular dysfunction. Aviat Space Environ Med 72, 567–575.

Zhang, L. F. (2001) Vascular adaptation to microgravity: what have we learned? Journal of Applied Physioloy, 91, 2415–2430.

Zupan, L. H., Peterka, R. J., and Merfeld, D. M. (2000) Neural processing of gravito-inertial cues in humans. I. Influence of the Semicircular canals following post-rotatory tilt, Journal of Neurophysiology 84 (4), 2001-2015.

Appendix A – Disqualifying medical conditions

Subject either reads this information or the experimenter asks the subject (adapted from Brown, 2002 and Sienko, 2000).

-Subject must be under 200lbs, between 5'2" and 6'0", and have abstained from caffeine use in the past 24 hours and alcohol use in the last 48 hours.

-Experiences with rotating devices, especially those used in a research environment.
-Possibility of pregnancy
-Any conditions that could be aggravated by motion sickness.
-Frequent or severe headaches
-Dizziness or fainting spells
-Paralysis
-Epilepsy
-Disturbances in consciousness
-Loss of control of nervous system functions
-Neurological problems
-Neuritis
-Loss of memory or amnesia
-Lazy eye
-Evident strabismus (cross-eye)
-Cylindrical contact lenses
-Reduced eye movements
-Astigmatism
-Ear, nose and throat trouble
-Hearing loss
-Chronic or frequent colds
-Head injury
-Asthma
-Shortness of breath
-Pain or pressure in the chest
-Medication (sedatives, anti-dizziness drugs, anti-depressants, BC allowed)
-Substance dependence or abuse (alcohol, marijuana, cocaine, hallucinogens, etc.)
-Diagnosis of psychosis, bipolar disorder or severe personality disorders
-Hear problems (angina pectoris, heart disease, past myocardial infarcations, valve replacement, pace makers)
-High or low blood pressure
-Recent loss or gain of weight
-High susceptibility to motion sickness
-Thyroid trouble
-Claustrophobia
-Inability to perform certain motions or assume certain positions

Appendix B - Consent form

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
MAN-VEHICLE LABORATORY
CONTEXT-SPECIFIC ADAPTATION OF OCULOMOTOR RESPONSES TO CENTRIFUGATION
CONSENT FORM

I have been asked to participate in a study on adaptation to movement in a rotating environment. I understand that participation is voluntary and that I may end my participation at any time for any reason. I understand that I should not participate in this study if I have any medical heart conditions, respiratory conditions, if I have any medical conditions which would be triggered if I develop motion sickness, if I am under the influence of alcohol, caffeine, anti-depressants, or sedatives, if I have suffered in the past from a serious head injury (concussion), or if there is any possibility that I may be pregnant. My participation as a subject on the MIT Artificial Gravity Simulator (AGS) involves either the testing of equipment or actual experimental trials. Prior to rotation on the AGS, I will be oriented to the rotator and data acquisition instrumentation. I understand that my height, weight, heart rate, blood pressure, and general medical history may be measured and recorded. During the experiment I will lie in either the supine, the prone position, or on the side on the rotator bed. If I am in the prone or side position my head will be supported by a pivoting, cushioned headrest. The headrest will allow me to make a free range of head movements to the left and the right, and I will be in full control of my head movements at all times. If I experience any discomfort from head movements while in either the prone or the supine position, I am free to discontinue the movements at any time. During the experiment, I will also wear eye imaging goggles. How this device will feel has been described to me. I agree to participate in possible stationary monitoring periods before and/or after rotation. My rotation on the AGS will not exceed the following parameters:

-acceleration no greater than 1 rpm/s
-G level at my feet no greater than 1.5 G
-time of rotation not exceeding 1 hour

I understand that these parameters are well within the safe limits for short-radius rotation. I can terminate rotation at any time by pressing the emergency stop button, the use of which has been demonstrated to me. I understand that during rotation I may develop a headache or feel pressure in my legs caused by a fluid shift due to centrifugation. I may also experience nausea or motion sickness, especially as a result of the required head movements. The experimenter may terminate the experiment if I report a pre-determined degree of motion sickness symptoms. In addition, I understand that my heart rate may increase due to the rotation speed; this is no greater than that sustained during aerobic exercise. I understand that serious injury could result from falling off the AGS while it is rotating. I will be loosely restrained at by a safety belt, which is to be worn around the waist/chest at all times while the AGS is rotating. In addition, the AGS is equipped with strong side railings similar to those on a hospital bed, and it is covered

by a steel-framed canopy. I will be continuously monitored by at least one experimenter in the same room. The investigator can also see me through a video camera mounted on the AGS, and in this way determine the nature of any problems that arise.

During and after the experiment I will be asked to report my subjective experience (how I feel, how I think I perceive my head movements, etc.). In addition, I will be asked to report a motion sickness rating during the experiment. This data will be recorded anonymously.

If I am a participant in experimental trials, I tentatively agree to return for additional trials (at most 10) requested by the experimenter. I understand that a possible protocol for an actual trial will consist of a short period of supine rest in the dark, followed by a period of head movements (ranging from 90 degrees to the left, to vertical, to 90 degrees to the right) in the dark, followed by a period of similar head movements in the light, and that this trial could be repeated many times. During these head movements, my head will move at approximately a speed of 0.25 meters per second.

In the unlikely event of physical injury resulting from participation in this research, I understand that medical treatment will be available from the MIT Medical Department, including first aid emergency treatment and follow-up care as needed, and that my insurance carrier may be billed for the cost of such treatment. However, no compensation can be provided for medical care apart from the foregoing. I further understand that making such medical treatment available, or providing it, does not imply that such injury is the investigator's fault. I also understand that by my participation in this study I am not waiving any of my legal rights (further information may be obtained by calling the Institute's Insurance and Legal Affairs Office at 253-2822). Monetary compensation for those who are not members of the Man-Vehicle Laboratory will be $10 per hour. Subjects from the Man-Vehicle Lab will be taken on a voluntary basis and will not be paid.

I understand that I may also contact the Chairman of the Committee on the Use of Humans as Experimental Subjects, Leigh Firn, M.D. (MIT E23-389, 253-6787), if I feel I have been treated unfairly as a subject. I have been informed as to the nature of and the purpose of this experiment and the risks involved, and agree to participate in the experiment. In case I experience any discomfort, I am free to discontinue the head-movements any time I wish to do so. I understand that I will receive a copy of this consent form.

Subject Date Experimenter

Appendix C – Instructions to subjects

During this experiment you will perform a series of head movements while rotating on the centrifuge. These head movements will consist of pitching your head forwards and backwards, and turning your head to the right and back up. These motions will be demonstrated to you and you will have a chance to practice them before the centrifuge starts spinning.

During most head movements you will experience an illusory sensation of your body rotating through space. For example, you may feel yourself pitching forward or rolling over to one side. After each head movement I will ask you to rate the overall intensity of the motion you are experiencing. The first time you pitch your head forward the intensity will be called a "10", and from then on, you will use a linear scale of 0-infinity to describe the intensity of your sensations for all other head motions.

Periodically you will be asked how motion sick you are. The motion sickness you report should be on a scale from 0-20, with 0 being normal, and 20 being "I'm about to vomit."

The head movements will be performed in blocks of six, with "one turn" being one motion forwards or backwards (for pitch movements), or one motion to the right or back to the nose-up position. The blocks will be performed in this order:

6 pitch turns (in darkness)
6 yaw turns (in darkness)
12 yaw turns (in light)
6 yaw turns (in darkness)
6 pitch turns (in darkness)

Your head will be unrestrained, but it is important that you try to make consistent motions within one plane in space. A metal bar above your head and a hat with a vertical rod will help guide your pitch turns. Additionally, for the pitch turns hold your head up with both hands to guide you, and to help keep your head in the up position for 30 seconds (the experimenter will tell you when to come back down).

Appendix D – Operator checklist/protocol

Before subject arrives:

1. Confirm goggles, lights, and camera are present and plugged in.
2. Check batteries, replace if necessary.
3. Turn on video camera.
4. Turn on all VCRs and monitors (confirm signals).
5. Turn on ISCAN computer (confirm signals).
6. Turn on data collection computer.
7. Bed controller OFF.
8. Secure bed.
9. Move footplate out.
10. Tidy bed.

When subject arrives:

1. Introduce subject to lab and overall experiment. Put up "do not enter" sign.
2. Ensure subject meets all medical requirements.
3. Subject signs consent form.
4. Subject reads instructions and receives detailed verbal explanations.
    a. Explain motion sickness scale.
    b. Explain illusory sensation scale.
    c. Explain timing of head turns.
    d. Explain need to perform turns in a consistent manner.
    e. Explain need to keep eyes wide open.
    f. Explain emergency stop button.
5. Subject dons pitch turn restraint hat.
6. Subject lies on bed and is centered with head-on-axis.
7. Help subject with putting on goggles. Turn on goggles.
8. Provide subject with blindfold.
9. Adjust pitch restraint bar and footplate.
10. Secure safety belt and position emergency stop switch within reach.
11. Add balance weights if needed (<130lbs, inside foot plate; >150lbs, at head)
12. Position calibration cross and calibrate goggles.
13. Readjust pitch restraint bar.
14. Practice pitch and yaw turns.
15. Measure pitch and yaw angles.
16. Cover centrifuge with canopy.
17. Emplace centrifuge cloth cover and ensure video signal is maintained.
18. Rotate bed once to ensure clearances.
19. Turn bed power switch ON.
20. Turn off lights and instruct subject to don blindfold.

21. Close curtain.
22. Ask subject to perform final practice pitch and yaw movement.
23. Ask subject if they are ready to begin.
24. Ramp up to 23rpm.
25. Phase 0 pitch turns.
26. Phase 0 yaw turns.
27. Yaw turns in light.
28. Phase 1 yaw turns.
29. Phase 1 pitch turns.
20. Stop centrifuge, power to OFF, and save ISCAN data immediately.
31. Help subject out of centrifuge.

After subject leaves:

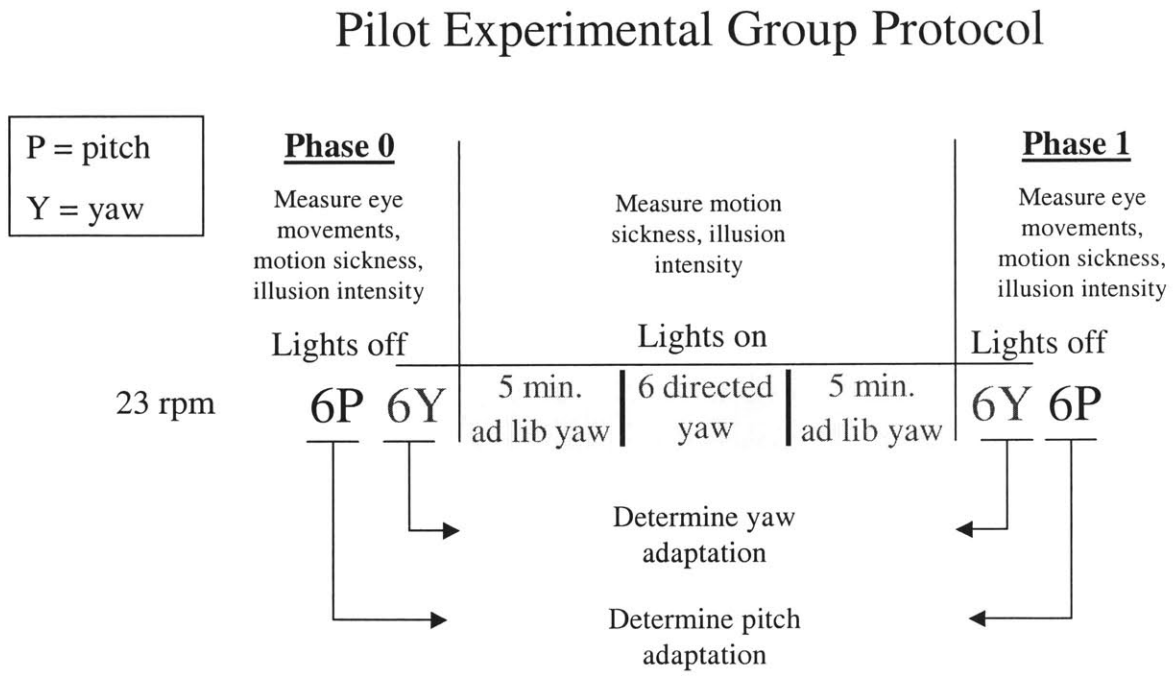
1. Turn off camera and recharge its battery.
2. Turn off goggles and ensure a fresh battery is charging.
3. Turn off all computers and monitors.
4. Remove "do not enter" sign.

Appendix E – Pilot study protocol

Below is a diagram depicting the protocol performed in a pilot study (compare with Figure 3.1). The major difference in this pilot study is that subjects are free to perform as many yaw movements as they wish during two five-minute blocks in the light. In addition, a set of six yaw movements is performed in between these two five-minute sessions. The protocol was to be performed over two days.

Five out of six subjects dropped out due to motion sickness. Subjects who dropped out completed a range of 18-58 *ad lib* head turns. A seventh subject was able to complete the protocol when only the first five minutes of *ad lib* yaw turns were performed.

A second pilot study conducted with three-minute long *ad lib* sessions and no block of pitch movements at the end of the first day was successful for two out of two subjects.



Appendix F – Subject data

Pitch head turns: *For the Experimental Group, only the maximum motion sickness score achieved within a six-turn block is reported.

SUB.	GENDER (0 = F 1 = M)	GROUP (0 = Control 1 = Exp.)	PITCH ANGLE (deg.)	DAY	PHASE	REP	DIRECT. (0 = to NU 1 = to NF)	TURN NUM	NSPV	TAU (sec.)	SICK*	ILLUS
102	1	1	45	0	0	0	1	1	0.17	12.93		10
102	1	1	45	0	0	0	0	2	0.15	13.55		10
102	1	1	45	0	0	1	1	3	0.18	20.69		6
102	1	1	45	0	0	1	0	4	0.18	15.49		6
102	1	1	45	0	0	2	1	5	0.17	19.67		6
102	1	1	45	0	0	2	0	6	0.20	19.10	5	5
102	1	1	45	0	1	0	1	7	0.18	9.50		5
102	1	1	45	0	1	0	0	8	0.18	9.92		6
102	1	1	45	0	1	1	1	9	0.17	21.77		4
102	1	1	45	0	1	1	0	10	0.22	16.51		4
102	1	1	45	0	1	2	1	11	0.19	16.89		5
102	1	1	45	0	1	2	0	12	0.26	14.49	12	1
102	1	1	45	1	0	0	1	13	0.19	12.77		6
102	1	1	45	1	0	0	0	14	0.29	16.02		7
102	1	1	45	1	0	1	1	15	0.16	21.94		6
102	1	1	45	1	0	1	0	16	0.26	15.74		6
102	1	1	45	1	0	2	1	17	0.21	15.48		5
102	1	1	45	1	0	2	0	18	0.27	16.32	2	5
102	1	1	45	1	1	0	1	19	0.15	16.43		6
102	1	1	45	1	1	0	0	20	0.23	20.41		5
102	1	1	45	1	1	1	1	21	0.24	18.98		5
102	1	1	45	1	1	1	0	22	0.29	16.28		4
102	1	1	45	1	1	2	1	23	0.21	14.44		3
102	1	1	45	1	1	2	0	24	0.24	15.47	16	0
103	1	1	35	0	0	0	1	1	0.13	8.80		10
103	1	1	35	0	0	0	0	2	0.18	11.64		11
103	1	1	35	0	0	1	1	3	0.15	8.16		11
103	1	1	35	0	0	1	0	4	0.19	10.00		12
103	1	1	35	0	0	2	1	5	0.18	8.19		11
103	1	1	35	0	0	2	0	6	0.21	9.26	0	13
103	1	1	35	0	1	0	1	7	0.18	8.77		12
103	1	1	35	0	1	0	0	8	0.18	9.92		11
103	1	1	35	0	1	1	1	9	0.16	8.08		11
103	1	1	35	0	1	1	0	10	0.18	10.92		12
103	1	1	35	0	1	2	1	11	0.17	8.30		11
103	1	1	35	0	1	2	0	12	0.17	9.94	1	10
103	1	1	35	1	0	0	1	13	0.23	9.68		10
103	1	1	35	1	0	0	0	14	0.23	10.62		12
103	1	1	35	1	0	1	1	15	0.20	10.76		12
103	1	1	35	1	0	1	0	16	0.23	8.91		11
103	1	1	35	1	0	2	1	17	0.23	9.07		12
103	1	1	35	1	0	2	0	18	0.17	9.09	0	12.5
103	1	1	35	1	1	0	1	19	0.23	10.05		12
103	1	1	35	1	1	0	0	20	0.23	10.77		15
103	1	1	35	1	1	1	1	21	0.23	8.54		13
103	1	1	35	1	1	1	0	22	0.13	12.61		14
103	1	1	35	1	1	2	1	23	0.24	7.17		15
103	1	1	35	1	1	2	0	24	0.17	10.29	0	14

105	0	1	50	0	0	0	1	1	0.22	17.15		10
105	0	1	50	0	0	0	0	2	0.12	11.55		8
105	0	1	50	0	0	1	1	3	0.22	13.48		10
105	0	1	50	0	0	1	0	4	0.21	8.66		10
105	0	1	50	0	0	2	1	5	0.22	16.73		10
105	0	1	50	0	0	2	0	6	0.18	11.29	4	11
105	0	1	50	0	1	0	1	7	0.26	10.57		18
105	0	1	50	0	1	0	0	8	0.18	10.65		18
105	0	1	50	0	1	1	1	9	0.19	12.96		15
105	0	1	50	0	1	1	0	10	0.15	13.52		15
105	0	1	50	0	1	2	1	11	0.20	9.99		15
105	0	1	50	0	1	2	0	12	0.15	11.64	10	18
105	0	1	50	1	0	0	1	13	0.47	8.55		10
105	0	1	50	1	0	0	0	14	0.56	4.50		10
105	0	1	50	1	0	1	1	15	0.45	17.32		10
105	0	1	50	1	0	1	0	16	0.35	12.34		10
105	0	1	50	1	0	2	1	17	0.52	9.55		10
105	0	1	50	1	0	2	0	18	0.50	13.38	0.5	10
105	0	1	50	1	1	0	1	19	0.58	6.00		7
105	0	1	50	1	1	0	0	20	0.68	9.68		10
105	0	1	50	1	1	1	1	21	0.46	5.12		6
105	0	1	50	1	1	1	0	22	0.55	10.99		10
105	0	1	50	1	1	2	1	23	0.31	7.12		5
105	0	1	50	1	1	2	0	24	0.67	8.40	2	10
106	1	1	45	0	0	0	1	1	0.48	21.15		10
106	1	1	45	0	0	0	0	2	0.47	12.89		11
106	1	1	45	0	0	1	1	3	0.51	14.91		8
106	1	1	45	0	0	1	0	4	0.67	10.32		9
106	1	1	45	0	0	2	1	5	0.50	11.86		9
106	1	1	45	0	0	2	0	6	0.57	8.64	1	8
106	1	1	45	0	1	0	1	7	0.64	13.95		6
106	1	1	45	0	1	0	0	8	0.70	10.40		6
106	1	1	45	0	1	1	1	9	0.59	11.37		5
106	1	1	45	0	1	1	0	10	0.66	10.13		4
106	1	1	45	0	1	2	1	11	0.64	11.60		4
106	1	1	45	0	1	2	0	12	0.70	11.04	4	3
106	1	1	45	1	0	0	1	13	0.24	12.04		3
106	1	1	45	1	0	0	0	14	0.25	15.54		5
106	1	1	45	1	0	1	1	15	0.82	11.65		5
106	1	1	45	1	0	1	0	16	0.83	14.15		4
106	1	1	45	1	0	2	1	17	0.70	12.64		4
106	1	1	45	1	0	2	0	18	0.96	11.27	0	4
106	1	1	45	1	1	0	1	19	0.79	13.41		2
106	1	1	45	1	1	0	0	20	0.90	10.68		3
106	1	1	45	1	1	1	1	21	0.72	10.98		1.7
106	1	1	45	1	1	1	0	22	1.01	10.65		3
106	1	1	45	1	1	2	1	23	0.86	10.74		1.5
106	1	1	45	1	1	2	0	24	0.97	10.31	2	2.5
112	0	1	55	0	0	0	1	1	0.43	7.30		10
112	0	1	55	0	0	0	0	2	0.63	5.54		12
112	0	1	55	0	0	1	1	3	0.72	4.88		10
112	0	1	55	0	0	1	0	4	0.81	5.79		12
112	0	1	55	0	0	2	1	5	0.73	5.44		10
112	0	1	55	0	0	2	0	6	1.10	3.88	3	11
112	0	1	55	0	1	0	1	7	0.77	3.95		8
112	0	1	55	0	1	0	0	8	1.23	5.01		6
112	0	1	55	0	1	1	1	9	0.64	5.79		9
112	0	1	55	0	1	1	0	10	0.99	3.96		4
112	0	1	55	0	1	2	1	11	1.27	3.24		9

112	0	1	55	0	1	2	0	12	0.40	3.47	16	5
112	0	1	55	1	0	0	1	13	0.25	3.86		7
112	0	1	55	1	0	0	0	14	0.41	5.03		8
112	0	1	55	1	0	1	1	15	0.56	4.52		6
112	0	1	55	1	0	1	0	16	0.53	3.86		7
112	0	1	55	1	0	2	1	17	0.44	2.76		5
112	0	1	55	1	0	2	0	18	0.65	1.90	1	6
112	0	1	55	1	1	0	1	19	0.28	3.63		4
112	0	1	55	1	1	0	0	20	0.59	2.99		4
112	0	1	55	1	1	1	1	21	0.51	2.43		7
112	0	1	55	1	1	1	0	22	0.49	1.62		3
112	0	1	55	1	1	2	1	23	0.70	1.49		4
112	0	1	55	1	1	2	0	24	0.74	1.19	4	2
114	0	1	55	0	0	0	1	1	0.16	14.60		10
114	0	1	55	0	0	0	0	2	0.36	12.11		10
114	0	1	55	0	0	1	1	3	0.23	12.43		8
114	0	1	55	0	0	1	0	4	0.52	12.34		12
114	0	1	55	0	0	2	1	5	0.24	10.42		7
114	0	1	55	0	0	2	0	6	0.29	10.39	4	12
114	0	1	55	0	1	0	1	7	0.41	7.64		7
114	0	1	55	0	1	0	0	8	0.39	9.34		12
114	0	1	55	0	1	1	1	9	0.31	6.44		10
114	0	1	55	0	1	1	0	10	0.37	9.39		10
114	0	1	55	0	1	2	1	11	0.28	11.85		9
114	0	1	55	0	1	2	0	12	0.39	8.46	11	8
114	0	1	55	1	0	0	1	13	0.16	12.80		10
114	0	1	55	1	0	0	0	14	0.33	9.62		10
114	0	1	55	1	0	1	1	15	0.22	11.98		10
114	0	1	55	1	0	1	0	16	0.28	9.19		8
114	0	1	55	1	0	2	1	17	0.26	12.11		9
114	0	1	55	1	0	2	0	18	0.28	10.28	5	6
114	0	1	55	1	1	0	1	19	0.39	11.30		10
114	0	1	55	1	1	0	0	20	0.33	8.35		8
114	0	1	55	1	1	1	1	21	0.32	7.82		8
114	0	1	55	1	1	1	0	22	0.36	6.88		7
114	0	1	55	1	1	2	1	23	0.32	8.95		10
114	0	1	55	1	1	2	0	24	0.33	5.74	11	8
116	1	1	55	0	0	0	1	1	0.58	17.78		10
116	1	1	55	0	0	0	0	2	0.88	10.60		9
116	1	1	55	0	0	1	1	3	0.74	13.69		8
116	1	1	55	0	0	1	0	4	0.83	8.96		8
116	1	1	55	0	0	2	1	5	0.77	13.22		8
116	1	1	55	0	0	2	0	6	0.78	8.53	2	6
116	1	1	55	0	1	0	1	7	0.65	11.26		6
116	1	1	55	0	1	0	0	8	0.63	8.68		6
116	1	1	55	0	1	1	1	9	0.73	11.15		6
116	1	1	55	0	1	1	0	10	0.81	7.81		5
116	1	1	55	0	1	2	1	11	0.71	12.15		4
116	1	1	55	0	1	2	0	12	0.59	6.92	7	4
116	1	1	55	1	0	0	1	13	0.75	12.13		10
116	1	1	55	1	0	0	0	14	0.88	9.08		8
116	1	1	55	1	0	1	1	15	0.75	11.36		9
116	1	1	55	1	0	1	0	16	0.68	10.52		8
116	1	1	55	1	0	2	1	17	0.67	12.13		8
116	1	1	55	1	0	2	0	18	0.76	8.45	1	7
116	1	1	55	1	1	0	1	19	0.80	8.60		6
116	1	1	55	1	1	0	0	20	0.78	8.64		5
116	1	1	55	1	1	1	1	21	0.64	11.65		5
116	1	1	55	1	1	1	0	22	0.46	9.39		5

116	1	1	55	1	1	2	1	23	0.68	10.60		6
116	1	1	55	1	1	2	0	24	0.83	6.92	4	4
118	0	1	55	0	0	0	1	1	0.09	13.49		10
118	0	1	55	0	0	0	0	2	0.22	7.93		12
118	0	1	55	0	0	1	1	3	0.16	6.85		10
118	0	1	55	0	0	1	0	4	0.19	6.31		12
118	0	1	55	0	0	2	1	5	0.17	6.18		8
118	0	1	55	0	0	2	0	6	0.28	5.95	2	10
118	0	1	55	0	1	0	1	7	0.21	4.68		10
118	0	1	55	0	1	0	0	8	0.20	4.17		18
118	0	1	55	0	1	1	1	9	0.17	7.48		12
118	0	1	55	0	1	1	0	10	0.20	3.92		18
118	0	1	55	0	1	2	1	11	0.27	5.02		14
118	0	1	55	0	1	2	0	12	0.15	6.93	4	14
118	0	1	55	1	0	0	1	13	0.11	4.99		10
118	0	1	55	1	0	0	0	14	0.20	5.40		11
118	0	1	55	1	0	1	1	15	0.14	7.34		13
118	0	1	55	1	0	1	0	16	0.22	7.53		11
118	0	1	55	1	0	2	1	17	0.16	5.05		14
118	0	1	55	1	0	2	0	18	0.22	5.63	2	12
118	0	1	55	1	1	0	1	19	0.16	5.36		14
118	0	1	55	1	1	0	0	20	0.17	6.22		13
118	0	1	55	1	1	1	1	21	0.13	5.61		11
118	0	1	55	1	1	1	0	22	0.19	6.87		12
118	0	1	55	1	1	2	1	23	0.14	6.27		12
118	0	1	55	1	1	2	0	24	0.20	7.72	4	14
120	0	1	55	0	0	0	1	1	0.54	7.33		10
120	0	1	55	0	0	0	0	2	0.46	5.59		10
120	0	1	55	0	0	1	1	3	0.46	8.11		9
120	0	1	55	0	0	1	0	4	0.63	6.64		9
120	0	1	55	0	0	2	1	5	0.47	5.89		12
120	0	1	55	0	0	2	0	6	0.52	7.27	5	12
120	0	1	55	0	1	0	1	7	0.39	5.06		12
120	0	1	55	0	1	0	0	8	0.34	6.40		13
120	0	1	55	0	1	1	1	9	0.26	5.71		12
120	0	1	55	0	1	1	0	10	0.33	6.46		12
120	0	1	55	0	1	2	1	11	0.25	11.43		12
120	0	1	55	0	1	2	0	12	0.28	5.84	6	11
120	0	1	55	1	0	0	1	13	0.72	7.16		5
120	0	1	55	1	0	0	0	14	0.57	5.96		5
120	0	1	55	1	0	1	1	15	0.56	7.84		6
120	0	1	55	1	0	1	0	16	0.56	6.61		5
120	0	1	55	1	0	2	1	17	0.52	6.88		7
120	0	1	55	1	0	2	0	18	0.49	7.18	1	6
120	0	1	55	1	1	0	1	19	0.65	5.84		10
120	0	1	55	1	1	0	0	20	0.51	6.17		10
120	0	1	55	1	1	1	1	21	0.32	4.26		10
120	0	1	55	1	1	1	0	22	0.46	4.02		9
120	0	1	55	1	1	2	1	23	0.38	3.98		10
120	0	1	55	1	1	2	0	24	0.35	6.37	4	9
124	0	1	65	0	0	0	1	1	0.34	12.51		10
124	0	1	65	0	0	0	0	2	0.56	10.10		9
124	0	1	65	0	0	1	1	3	0.31	13.35		10
124	0	1	65	0	0	1	0	4	0.34	13.65		10
124	0	1	65	0	0	2	1	5	0.38	12.59		11
124	0	1	65	0	0	2	0	6	0.64	9.21	1	10
124	0	1	65	0	1	0	1	7	0.49	12.41		11
124	0	1	65	0	1	0	0	8	0.47	9.22		11
124	0	1	65	0	1	1	1	9	0.29	11.28		12

124	0	1	65	0	1	1	0	10	0.49	8.87		9
124	0	1	65	0	1	2	1	11	0.48	9.17		10
124	0	1	65	0	1	2	0	12	0.56	8.24	4	9
124	0	1	65	1	0	0	1	13	0.23	13.06		5
124	0	1	65	1	0	0	0	14	0.31	8.53		6
124	0	1	65	1	0	1	1	15	0.25	12.03		6
124	0	1	65	1	0	1	0	16	0.32	8.81		6
124	0	1	65	1	0	2	1	17	0.22	9.16		5
124	0	1	65	1	0	2	0	18	0.30	8.59	0	6
124	0	1	65	1	1	0	1	19	0.38	6.45		8
124	0	1	65	1	1	0	0	20	0.37	3.60		9
124	0	1	65	1	1	1	1	21	0.19	5.55		8
124	0	1	65	1	1	1	0	22	0.25	7.52		9
124	0	1	65	1	1	2	1	23	0.11	4.42		8
124	0	1	65	1	1	2	0	24	0.32	6.51	1	8
7	1	0	50	0	0	0	1	1	0.35	12.27	0	10
7	1	0	50	0	0	0	0	2	0.23	19.95	2	6
7	1	0	50	0	0	1	1	3	0.28	19.37	0	7
7	1	0	50	0	0	1	0	4	0.19	21.50	0	10
7	1	0	50	0	0	2	1	5	0.30	16.75	0	10
7	1	0	50	0	0	2	0	6	0.26	15.55	2	7
7	1	0	50	0	1	0	1	7	0.27	10.25	3	12
7	1	0	50	0	1	0	0	8	0.15	11.35	2	10
7	1	0	50	0	1	1	1	9	0.34	12.48	3	12
7	1	0	50	0	1	1	0	10	0.31	15.42	3	8
7	1	0	50	0	1	2	1	11	0.41	9.53	2	6
7	1	0	50	0	1	2	0	12	0.36	14.14	2	12
7	1	0	50	1	0	0	1	13	0.37	14.73	0	12
7	1	0	50	1	0	0	0	14	0.35	15.00	0	6
7	1	0	50	1	0	1	1	15	0.37	14.06	0	10
7	1	0	50	1	0	1	0	16	0.42	15.66	2	8
7	1	0	50	1	0	2	1	17	0.43	16.38	3	12
7	1	0	50	1	0	2	0	18	0.38	17.48	3	8
7	1	0	50	1	1	0	1	19	0.43	11.86	0	12
7	1	0	50	1	1	0	0	20	0.46	11.63	3	12
7	1	0	50	1	1	1	1	21	0.42	11.57	3	8
7	1	0	50	1	1	1	0	22	0.34	11.69	3	8
7	1	0	50	1	1	2	1	23	0.43	11.74	3	8
7	1	0	50	1	1	2	0	24	0.43	12.74	3	8
8	0	0	50	0	0	0	1	1	0.57	15.23	0	10
8	0	0	50	0	0	0	0	2	0.24	13.06	0	10
8	0	0	50	0	0	1	1	3	0.61	10.84	0	18
8	0	0	50	0	0	1	0	4	0.59	11.32	0	15
8	0	0	50	0	0	2	1	5	0.58	12.08	0	15
8	0	0	50	0	0	2	0	6	0.45	13.01	0	12
8	0	0	50	0	1	0	1	7	0.56	11.22	0	20
8	0	0	50	0	1	0	0	8	0.66	8.87	0	12
8	0	0	50	0	1	1	1	9	0.54	8.54	0	18
8	0	0	50	0	1	1	0	10	0.51	10.68	0	5
8	0	0	50	0	1	2	1	11	0.31	12.09	0	15
8	0	0	50	0	1	2	0	12	0.72	9.01	0	5
8	0	0	50	1	0	0	1	13	0.49	12.30	0	15
8	0	0	50	1	0	0	0	14	0.43	12.42	0	2
8	0	0	50	1	0	1	1	15	0.40	9.89	0	10
8	0	0	50	1	0	1	0	16	0.35	13.08	0	5
8	0	0	50	1	0	2	1	17	0.34	9.02	0	10
8	0	0	50	1	0	2	0	18	0.44	12.39	0	5
8	0	0	50	1	1	0	1	19	0.47	10.04	0	10
8	0	0	50	1	1	0	0	20	0.24	15.84	0	8

8	0	0	50	1	1	1	1	21	0.49	10.11	0	12
8	0	0	50	1	1	1	0	22	0.43	9.85	0	8
8	0	0	50	1	1	2	1	23	0.49	8.45	0	15
8	0	0	50	1	1	2	0	24	0.27	10.29	0	8
12	1	0	65	0	0	0	1	1	0.42	8.29	0	10
12	1	0	65	0	0	0	0	2	0.31	9.77	0	10
12	1	0	65	0	0	1	1	3	0.36	9.09	0	8
12	1	0	65	0	0	1	0	4	0.33	9.77	1	12
12	1	0	65	0	0	2	1	5	0.32	8.65	0	6
12	1	0	65	0	0	2	0	6	0.30	12.67	1	10
12	1	0	65	0	1	0	1	7	0.48	11.87	1	12
12	1	0	65	0	1	0	0	8	0.33	12.51	3	13
12	1	0	65	0	1	1	1	9	0.48	8.76	3	10
12	1	0	65	0	1	1	0	10	0.17	8.03	3	13
12	1	0	65	0	1	2	1	11	0.36	7.68	2	12
12	1	0	65	0	1	2	0	12	0.28	8.37	4	13
12	1	0	65	1	0	0	1	13	0.46	8.83	0	8
12	1	0	65	1	0	0	0	14	0.41	11.20	0	10
12	1	0	65	1	0	1	1	15	0.44	8.88	0	8
12	1	0	65	1	0	1	0	16	0.37	9.96	0	10
12	1	0	65	1	0	2	1	17	0.36	9.11	0	6
12	1	0	65	1	0	2	0	18	0.39	10.06	0	10
12	1	0	65	1	1	0	1	19	0.42	8.33	1	8
12	1	0	65	1	1	0	0	20	0.38	8.21	1	10
12	1	0	65	1	1	1	1	21	0.42	8.19	1	8
12	1	0	65	1	1	1	0	22	0.33	9.33	2	11
12	1	0	65	1	1	2	1	23	0.41	7.99	1	10
12	1	0	65	1	1	2	0	24	0.28	7.69	0	10
13	0	0	65	0	0	0	1	1	0.31	15.60	0	10
13	0	0	65	0	0	0	0	2	0.30	9.68	0	10
13	0	0	65	0	0	1	1	3	0.34	10.96	0	10
13	0	0	65	0	0	1	0	4	0.31	10.75	0	10
13	0	0	65	0	0	2	1	5	0.32	11.57	2	11
13	0	0	65	0	0	2	0	6	0.28	10.18	2	9
13	0	0	65	0	1	0	1	7	0.34	11.33	2	11
13	0	0	65	0	1	0	0	8	0.24	7.03	2	9
13	0	0	65	0	1	1	1	9	0.39	8.73	2	10
13	0	0	65	0	1	1	0	10	0.25	8.66	3	8
13	0	0	65	0	1	2	1	11	0.34	7.59	3	9
13	0	0	65	0	1	2	0	12	0.28	7.25	3	7
13	0	0	65	1	0	0	1	13	0.48	14.63	0	12
13	0	0	65	1	0	0	0	14	0.30	8.80	0	11
13	0	0	65	1	0	1	1	15	0.46	10.27	0	12
13	0	0	65	1	0	1	0	16	0.35	9.39	1	12
13	0	0	65	1	0	2	1	17	0.44	8.02	1	12
13	0	0	65	1	0	2	0	18	0.30	10.07	1	6
13	0	0	65	1	1	0	1	19	0.44	10.65	4	11
13	0	0	65	1	1	0	0	20	0.32	10.89	4	8
13	0	0	65	1	1	1	1	21	0.47	7.80	5	10
13	0	0	65	1	1	1	0	22	0.30	7.86	5	8
13	0	0	65	1	1	2	1	23	0.40	7.09	5	10
13	0	0	65	1	1	2	0	24	0.33	8.25	5	7
15	1	0	70	0	0	0	1	1	0.32	7.63	0	10
15	1	0	70	0	0	0	0	2	0.26	7.35	0	11
15	1	0	70	0	0	1	1	3	0.41	7.38	0	13
15	1	0	70	0	0	1	0	4	0.29	6.55	0	10
15	1	0	70	0	0	2	1	5	0.46	6.36	0	13
15	1	0	70	0	0	2	0	6	0.31	5.21	1	10
15	1	0	70	0	1	0	1	7	0.33	8.28	0	9

15	1	0	70	0	1	0	0	8	0.28	3.75	0	8
15	1	0	70	0	1	1	1	9	0.39	6.46	4	8
15	1	0	70	0	1	1	0	10	0.37	5.45	0	7
15	1	0	70	0	1	2	1	11	0.48	5.96	0	7
15	1	0	70	0	1	2	0	12	0.31	6.14	0	6
15	1	0	70	1	0	0	1	13	0.40	7.28	0	6
15	1	0	70	1	0	0	0	14	0.36	5.69	0	5
15	1	0	70	1	0	1	1	15	0.43	7.20	0	5
15	1	0	70	1	0	1	0	16	0.37	5.54	0	4
15	1	0	70	1	0	2	1	17	0.54	6.42	0	5
15	1	0	70	1	0	2	0	18	0.37	5.85	0	4
15	1	0	70	1	1	0	1	19	0.39	6.86	3	5
15	1	0	70	1	1	0	0	20	0.42	4.50	0	3
15	1	0	70	1	1	1	1	21	0.43	6.00	0	3
15	1	0	70	1	1	1	0	22	0.40	4.86	0	2
15	1	0	70	1	1	2	1	23	0.54	5.79	0	3
15	1	0	70	1	1	2	0	24	0.37	5.95	0	2
16	1	0	65	0	0	0	1	1	0.24	8.48	0	10
16	1	0	65	0	0	0	0	2	0.25	7.27	0	12
16	1	0	65	0	0	1	1	3	0.30	7.20	0	10
16	1	0	65	0	0	1	0	4	0.33	6.54	4	12
16	1	0	65	0	0	2	1	5	0.35	7.65	0	14
16	1	0	65	0	0	2	0	6	0.27	7.24	0	11
16	1	0	65	0	1	0	1	7	0.34	6.41	4	12
16	1	0	65	0	1	0	0	8	0.30	4.92	6	11
16	1	0	65	0	1	1	1	9	0.31	7.90	8	14
16	1	0	65	0	1	1	0	10	0.24	5.78	8	11
16	1	0	65	0	1	2	1	11	0.35	6.48	8	9
16	1	0	65	0	1	2	0	12	0.34	3.46	8	11
16	1	0	65	1	0	0	1	13	0.19	7.76	0	6
16	1	0	65	1	0	0	0	14	0.15	2.65	0	10
16	1	0	65	1	0	1	1	15	0.19	7.26	0	7
16	1	0	65	1	0	1	0	16	0.50	2.23	1	9
16	1	0	65	1	0	2	1	17	0.24	4.88	0	7
16	1	0	65	1	0	2	0	18	0.33	5.54	0	7
16	1	0	65	1	1	0	1	19	0.26	4.06	0	8
16	1	0	65	1	1	0	0	20	0.17	5.30	0	8
16	1	0	65	1	1	1	1	21	0.30	5.26	3	8
16	1	0	65	1	1	1	0	22	0.27	2.84	1	9
16	1	0	65	1	1	2	1	23	0.29	4.09	7	7
16	1	0	65	1	1	2	0	24	0.22	2.90	7	9
17	1	0	45	0	0	0	1	1	0.19	20.86	1	10
17	1	0	45	0	0	0	0	2	0.28	12.70	1	11
17	1	0	45	0	0	1	1	3	0.26	17.65	1	10
17	1	0	45	0	0	1	0	4	0.31	11.66	1	9
17	1	0	45	0	0	2	1	5	0.27	15.92	1	9
17	1	0	45	0	0	2	0	6	0.33	11.45	1	8
17	1	0	45	0	1	0	1	7	0.32	13.70	0	7
17	1	0	45	0	1	0	0	8	0.32	9.59	0	6
17	1	0	45	0	1	1	1	9	0.30	14.70	0	4
17	1	0	45	0	1	1	0	10	0.34	10.32	0	5
17	1	0	45	0	1	2	1	11	0.31	12.93	0	4
17	1	0	45	0	1	2	0	12	0.31	10.87	0	3
17	1	0	45	1	0	0	1	13	0.26	15.44	1	9
17	1	0	45	1	0	0	0	14	0.35	12.69	1	11
17	1	0	45	1	0	1	1	15	0.35	14.07	1	9
17	1	0	45	1	0	1	0	16	0.29	14.86	1	8
17	1	0	45	1	0	2	1	17	0.35	13.95	1	7
17	1	0	45	1	0	2	0	18	0.39	12.21	1	8

17	1	0	45	1	1	0	1	19	0.46	12.65	1	8
17	1	0	45	1	1	0	0	20	0.37	10.98	1	7
17	1	0	45	1	1	1	1	21	0.36	13.97	1	5
17	1	0	45	1	1	1	0	22	0.35	13.53	1	6
17	1	0	45	1	1	2	1	23	0.36	13.29	1	4
17	1	0	45	1	1	2	0	24	0.33	13.10	1	3
18	1	0	55	0	0	0	1	1	0.50	9.84	0	10
18	1	0	55	0	0	0	0	2	0.42	7.95	0	10
18	1	0	55	0	0	1	1	3	0.38	8.73	0	13
18	1	0	55	0	0	1	0	4	0.51	9.65	0	10
18	1	0	55	0	0	2	1	5	0.47	6.49	0	5
18	1	0	55	0	0	2	0	6	0.51	7.35	0	5
18	1	0	55	0	1	0	1	7	0.37	6.11	0	13
18	1	0	55	0	1	0	0	8	0.30	7.24	0	10
18	1	0	55	0	1	1	1	9	0.37	4.25	0	5
18	1	0	55	0	1	1	0	10	0.46	6.93	0	5
18	1	0	55	0	1	2	1	11	0.38	6.93	0	0
18	1	0	55	0	1	2	0	12	0.52	8.97	0	0
18	1	0	55	1	0	0	1	13	0.38	6.25	0	12
18	1	0	55	1	0	0	0	14	0.42	8.43	0	12
18	1	0	55	1	0	1	1	15	0.35	6.31	0	12
18	1	0	55	1	0	1	0	16	0.22	7.63	0	12
18	1	0	55	1	0	2	1	17	0.34	6.01	0	8
18	1	0	55	1	0	2	0	18	0.16	6.67	0	10
18	1	0	55	1	1	0	1	19	0.31	5.19	0	5
18	1	0	55	1	1	0	0	20	0.37	7.09	0	5
18	1	0	55	1	1	1	1	21	0.27	5.98	0	8
18	1	0	55	1	1	1	0	22	0.32	8.18	0	5
18	1	0	55	1	1	2	1	23	0.38	6.51	0	2
18	1	0	55	1	1	2	0	24	0.32	6.44	0	0
19	1	0	55	0	0	0	1	1	0.39	6.64	0	10
19	1	0	55	0	0	0	0	2	0.30	8.75	0	15
19	1	0	55	0	0	1	1	3	0.30	6.28	0	13
19	1	0	55	0	0	1	0	4	0.34	6.90	0	17
19	1	0	55	0	0	2	1	5	0.28	6.50	0	19
19	1	0	55	0	0	2	0	6	0.27	5.79	1	22
19	1	0	55	0	1	0	1	7	0.35	6.75	0	10
19	1	0	55	0	1	0	0	8	0.37	8.62	0	18
19	1	0	55	0	1	1	1	9	0.30	5.77	1	14
19	1	0	55	0	1	1	0	10	0.25	6.47	2	25
19	1	0	55	0	1	2	1	11	0.22	5.51	1	16
19	1	0	55	0	1	2	0	12	0.28	8.19	3	22
19	1	0	55	1	0	0	1	13	0.25	6.26	0	12
19	1	0	55	1	0	0	0	14	0.22	7.87	0	14
19	1	0	55	1	0	1	1	15	0.26	5.19	0	13
19	1	0	55	1	0	1	0	16	0.24	5.13	0	15
19	1	0	55	1	0	2	1	17	0.23	5.69	0	13
19	1	0	55	1	0	2	0	18	0.24	5.04	0	14
19	1	0	55	1	1	0	1	19	0.32	7.99	0	12
19	1	0	55	1	1	0	0	20	0.28	5.94	0	15
19	1	0	55	1	1	1	1	21	0.15	6.42	0	10
19	1	0	55	1	1	1	0	22	0.24	7.48	0	14
19	1	0	55	1	1	2	1	23	0.19	4.20	0	16
19	1	0	55	1	1	2	0	24	0.25	6.58	0	11
20	0	0	55	0	0	0	1	1	0.36	9.74	0	10
20	0	0	55	0	0	0	0	2	0.39	10.36	0	11
20	0	0	55	0	0	1	1	3	0.32	7.88	0	10
20	0	0	55	0	0	1	0	4	0.35	9.23	0	10
20	0	0	55	0	0	2	1	5	0.34	7.54	0	10

20	0	0	55	0	0	2	0	6	0.41	8.85	0	10
20	0	0	55	0	1	0	1	7	0.41	7.20	0	10
20	0	0	55	0	1	0	0	8	0.31	7.82	0	9
20	0	0	55	0	1	1	1	9	0.32	7.24	0	9
20	0	0	55	0	1	1	0	10	0.43	7.55	0	9
20	0	0	55	0	1	2	1	11	0.32	6.04	0	10
20	0	0	55	0	1	2	0	12	0.37	7.03	0	9
20	0	0	55	1	0	0	1	13	0.30	9.63	0	10
20	0	0	55	1	0	0	0	14	0.34	7.15	0	9
20	0	0	55	1	0	1	1	15	0.31	6.02	0	10
20	0	0	55	1	0	1	0	16	0.30	7.88	0	10
20	0	0	55	1	0	2	1	17	0.26	10.14	0	9
20	0	0	55	1	0	2	0	18	0.29	8.93	0	8
20	0	0	55	1	1	0	1	19	0.31	7.59	0	9
20	0	0	55	1	1	0	0	20	0.30	7.95	0	7
20	0	0	55	1	1	1	1	21	0.33	6.90	0	9
20	0	0	55	1	1	1	0	22	0.36	6.43	0	7
20	0	0	55	1	1	2	1	23	0.28	7.46	1	9
20	0	0	55	1	1	2	0	24	0.33	7.43	0	7

Yaw head turns: All values are from the Experimental Group. *Only the maximum motion sickness score achieved within a six-turn block is reported.

SUB.	GENDER (0 = F 1 = M)	GROUP (All Exp.)	YAW ANGLE (deg.)	DAY	PHASE	REP	DIRECT. (1 = to RED 0 = to NU)	TURN NUM	NSPV	TAU (sec.)	SICK*	ILLUS
2	1	1	75	0	0	0	1	1	0.25	5.75		5
2	1	1	75	0	0	0	0	2	0.21	3.97		7
2	1	1	75	0	0	1	1	3	0.28	5.16		5
2	1	1	75	0	0	1	0	4	0.35	3.09		7
2	1	1	75	0	0	2	1	5	0.32	6.19		4
2	1	1	75	0	0	2	0	6	0.60	3.96	7	9
2	1	1	75	0	1	0	1	7	0.24	6.20		1
2	1	1	75	0	1	0	0	8	0.31	5.04		6
2	1	1	75	0	1	1	1	9	0.25	6.16		1
2	1	1	75	0	1	1	0	10	0.28	3.72		6
2	1	1	75	0	1	2	1	11	0.23	3.16		0
2	1	1	75	0	1	2	0	12	0.24	7.34	16	6
2	1	1	75	1	0	0	1	13	0.26	5.20		5
2	1	1	75	1	0	0	0	14	0.49	6.09		8
2	1	1	75	1	0	1	1	15	0.26	4.79		4
2	1	1	75	1	0	1	0	16	0.36	6.61		8
2	1	1	75	1	0	2	1	17	0.26	5.38		3
2	1	1	75	1	0	2	0	18	0.35	5.89	4	7
2	1	1	75	1	1	0	1	19	0.29	4.29		1
2	1	1	75	1	1	0	0	20	0.46	5.40		5
2	1	1	75	1	1	1	1	21	0.25	5.05		0
2	1	1	75	1	1	1	0	22	0.30	4.33		5
2	1	1	75	1	1	2	1	23	0.32	3.97		0
2	1	1	75	1	1	2	0	24	0.37	4.56	11	4
3	1	1	70	0	0	0	1	1	0.27	6.12		15
3	1	1	70	0	0	0	0	2	0.35	5.79		17
3	1	1	70	0	0	1	1	3	0.34	7.58		15
3	1	1	70	0	0	1	0	4	0.31	6.84		18
3	1	1	70	0	0	2	1	5	0.37	6.40		15
3	1	1	70	0	0	2	0	6	0.25	8.04	0	16
3	1	1	70	0	1	0	1	7	0.28	3.93		11
3	1	1	70	0	1	0	0	8	0.18	8.11		13
3	1	1	70	0	1	1	1	9	0.22	5.43		12
3	1	1	70	0	1	1	0	10	0.14	5.49		14
3	1	1	70	0	1	2	1	11	0.28	5.13		12
3	1	1	70	0	1	2	0	12	0.18	7.13	2	13
3	1	1	70	1	0	0	1	13	0.26	4.19		12
3	1	1	70	1	0	0	0	14	0.19	3.59		14
3	1	1	70	1	0	1	1	15	0.29	4.29		13
3	1	1	70	1	0	1	0	16	0.21	4.92		13
3	1	1	70	1	0	2	1	17	0.37	4.75		13
3	1	1	70	1	0	2	0	18	0.21	4.98	0	14
3	1	1	70	1	1	0	1	19	0.19	3.23		12
3	1	1	70	1	1	0	0	20	0.19	3.56		13
3	1	1	70	1	1	1	1	21	0.26	5.09		15
3	1	1	70	1	1	1	0	22	0.14	5.19		14
3	1	1	70	1	1	2	1	23	0.25	4.44		13
3	1	1	70	1	1	2	0	24	0.14	4.76	0	14
5	0	1	65	0	0	0	1	1	0.23	4.09		7
5	0	1	65	0	0	0	0	2	0.41	6.86		18
5	0	1	65	0	0	1	1	3	0.27	4.70		8
5	0	1	65	0	0	1	0	4	0.42	8.67		18

5	0	1	65	0	0	2	1	5	0.27	4.82		7
5	0	1	65	0	0	2	0	6	0.42	10.83	5	15
5	0	1	65	0	1	0	1	7	0.17	4.85		10
5	0	1	65	0	1	0	0	8	0.46	7.86		16
5	0	1	65	0	1	1	1	9	0.31	2.74		10
5	0	1	65	0	1	1	0	10	0.28	5.23		17
5	0	1	65	0	1	2	1	11	0.32	2.18		10
5	0	1	65	0	1	2	0	12	0.33	7.77	6	18
5	0	1	65	1	0	0	1	13	0.20	3.68		5
5	0	1	65	1	0	0	0	14	0.25	9.02		12
5	0	1	65	1	0	1	1	15	0.35	2.65		5
5	0	1	65	1	0	1	0	16	0.32	2.90		12
5	0	1	65	1	0	2	1	17	0.29	3.15		4
5	0	1	65	1	0	2	0	18	0.29	4.29	0.5	10
5	0	1	65	1	1	0	1	19	0.18	5.51		4
5	0	1	65	1	1	0	0	20	0.22	6.24		10
5	0	1	65	1	1	1	1	21	0.12	5.05		3
5	0	1	65	1	1	1	0	22	0.13	3.59		10
5	0	1	65	1	1	2	1	23	0.24	3.27		4
5	0	1	65	1	1	2	0	24	0.24	5.91	1.5	10
6	1	1	65	0	0	0	1	1	0.33	6.90		9
6	1	1	65	0	0	0	0	2	0.58	6.11		14
6	1	1	65	0	0	1	1	3	0.59	6.85		9
6	1	1	65	0	0	1	0	4	0.78	6.52		14
6	1	1	65	0	0	2	1	5	0.59	6.83		8
6	1	1	65	0	0	2	0	6	0.77	7.22	1	13
6	1	1	65	0	1	0	1	7	0.46	3.96		5
6	1	1	65	0	1	0	0	8	0.37	4.22		10
6	1	1	65	0	1	1	1	9	0.42	4.50		4
6	1	1	65	0	1	1	0	10	0.52	5.68		7
6	1	1	65	0	1	2	1	11	0.32	5.04		4
6	1	1	65	0	1	2	0	12	0.48	5.12	1	6
6	1	1	65	1	0	0	1	13	0.50	3.52		4
6	1	1	65	1	0	0	0	14	0.55	5.37		6
6	1	1	65	1	0	1	1	15	0.39	4.79		3.5
6	1	1	65	1	0	1	0	16	0.53	5.29		4.5
6	1	1	65	1	0	2	1	17	0.41	6.16		3
6	1	1	65	1	0	2	0	18	0.51	5.90	0	4
6	1	1	65	1	1	0	1	19	0.37	4.47		1.5
6	1	1	65	1	1	0	0	20	0.60	5.27		2.5
6	1	1	65	1	1	1	1	21	0.43	3.47		2
6	1	1	65	1	1	1	0	22	0.64	4.39		2.3
6	1	1	65	1	1	2	1	23	0.38	4.00		1.7
6	1	1	65	1	1	2	0	24	0.49	5.47	0.5	2
12	0	1	65	0	0	0	1	1	0.39	6.04		13
12	0	1	65	0	0	0	0	2	0.59	5.04		14
12	0	1	65	0	0	1	1	3	0.21	3.11		14
12	0	1	65	0	0	1	0	4	1.24	2.80		16
12	0	1	65	0	0	2	1	5	0.65	2.53		12
12	0	1	65	0	0	2	0	6	1.06	4.93	5	16
12	0	1	65	0	1	0	1	7	0.54	1.48		2
12	0	1	65	0	1	0	0	8	0.58	4.02		10
12	0	1	65	0	1	1	1	9	0.76	1.46		8
12	0	1	65	0	1	1	0	10	0.78	4.65		10
12	0	1	65	0	1	2	1	11	0.41	3.81		8
12	0	1	65	0	1	2	0	12	0.63	4.32	6	9
12	0	1	65	1	0	0	1	13	0.29	2.24		6
12	0	1	65	1	0	0	0	14	0.17	3.18		10
12	0	1	65	1	0	1	1	15	0.30	2.74		5

12	0	1	65	1	0	1	0	16	0.31	4.50		10
12	0	1	65	1	0	2	1	17	0.17	5.78		4
12	0	1	65	1	0	2	0	18	0.21	3.14	2	9
12	0	1	65	1	1	0	1	19	0.20	1.01		2
12	0	1	65	1	1	0	0	20	0.30	1.10		5
12	0	1	65	1	1	1	1	21	0.03	2.34		4
12	0	1	65	1	1	1	0	22	0.27	3.22		6
12	0	1	65	1	1	2	1	23	0.17	2.36		3
12	0	1	65	1	1	2	0	24	0.20	2.55	4	8
14	0	1	80	0	0	0	1	1	0.17	7.00		6
14	0	1	80	0	0	0	0	2	0.26	3.07		10
14	0	1	80	0	0	1	1	3	0.17	7.68		6
14	0	1	80	0	0	1	0	4	0.26	5.11		11
14	0	1	80	0	0	2	1	5	0.23	8.68		8
14	0	1	80	0	0	2	0	6	0.26	5.95	4	9
14	0	1	80	0	1	0	1	7	0.13	6.40		7
14	0	1	80	0	1	0	0	8	0.19	3.08		9
14	0	1	80	0	1	1	1	9	0.16	5.31		4
14	0	1	80	0	1	1	0	10	0.21	4.32		8
14	0	1	80	0	1	2	1	11	0.17	8.44		5
14	0	1	80	0	1	2	0	12	0.49	3.37	7	8
14	0	1	80	1	0	0	1	13	0.11	7.83		7
14	0	1	80	1	0	0	0	14	0.29	3.00		7
14	0	1	80	1	0	1	1	15	0.07	10.29		7
14	0	1	80	1	0	1	0	16	0.32	2.55		10
14	0	1	80	1	0	2	1	17	0.12	9.49		6
14	0	1	80	1	0	2	0	18	0.35	4.07	7	8
14	0	1	80	1	1	0	1	19	0.18	3.24		4
14	0	1	80	1	1	0	0	20	0.10	8.24		6
14	0	1	80	1	1	1	1	21	0.09	8.29		4
14	0	1	80	1	1	1	0	22	0.11	4.20		7
14	0	1	80	1	1	2	1	23	0.11	7.78		4
14	0	1	80	1	1	2	0	24	0.11	5.99	8	6
16	1	1	80	0	0	0	1	1	0.29	5.65		6
16	1	1	80	0	0	0	0	2	0.44	5.00		5
16	1	1	80	0	0	1	1	3	0.31	5.34		5
16	1	1	80	0	0	1	0	4	0.33	3.25		5
16	1	1	80	0	0	2	1	5	0.34	4.53		5
16	1	1	80	0	0	2	0	6	0.33	3.77	2	6
16	1	1	80	0	1	0	1	7	0.15	4.88		4
16	1	1	80	0	1	0	0	8	0.26	1.25		5
16	1	1	80	0	1	1	1	9	0.20	3.94		4
16	1	1	80	0	1	1	0	10	0.37	3.59		5
16	1	1	80	0	1	2	1	11	0.35	4.44		4
16	1	1	80	0	1	2	0	12	0.20	2.90	5	5
16	1	1	80	1	0	0	1	13	0.51	4.43		5
16	1	1	80	1	0	0	0	14	0.29	2.44		7
16	1	1	80	1	0	1	1	15	0.39	5.65		4
16	1	1	80	1	0	1	0	16	0.25	4.28		6
16	1	1	80	1	0	2	1	17	0.38	3.84		3
16	1	1	80	1	0	2	0	18	0.32	3.45	1	5
16	1	1	80	1	1	0	1	19	0.49	4.36		2
16	1	1	80	1	1	0	0	20	0.26	4.56		4
16	1	1	80	1	1	1	1	21	0.17	4.46		2
16	1	1	80	1	1	1	0	22	0.25	3.39		4
16	1	1	80	1	1	2	1	23	0.37	3.32		2
16	1	1	80	1	1	2	0	24	0.44	2.66	2	3
18	0	1	80	0	0	0	1	1	0.18	1.92		12
18	0	1	80	0	0	0	0	2	0.41	8.64		14

18	0	1	80	0	0	1	1	3	0.33	3.70		10
18	0	1	80	0	0	1	0	4	0.42	6.75		12
18	0	1	80	0	0	2	1	5	0.32	2.34		10
18	0	1	80	0	0	2	0	6	0.47	7.14	2	12
18	0	1	80	0	1	0	1	7	0.22	3.03		8
18	0	1	80	0	1	0	0	8	0.47	4.55		10
18	0	1	80	0	1	1	1	9	0.27	2.37		8
18	0	1	80	0	1	1	0	10	0.49	4.69		10
18	0	1	80	0	1	2	1	11	0.21	3.52		6
18	0	1	80	0	1	2	0	12	0.34	7.33	3	12
18	0	1	80	1	0	0	1	13	0.31	0.99		8
18	0	1	80	1	0	0	0	14	0.26	4.69		14
18	0	1	80	1	0	1	1	15	0.49	2.04		8
18	0	1	80	1	0	1	0	16	0.20	6.06		13
18	0	1	80	1	0	2	1	17	0.35	1.66		9
18	0	1	80	1	0	2	0	18	0.15	10.68	4	15
18	0	1	80	1	1	0	1	19	0.40	1.81		8
18	0	1	80	1	1	0	0	20	0.18	6.48		11
18	0	1	80	1	1	1	1	21	0.39	1.85		9
18	0	1	80	1	1	1	0	22	0.09	5.83		11
18	0	1	80	1	1	2	1	23	0.35	1.92		9
18	0	1	80	1	1	2	0	24	0.19	3.98	4	14
20	0	1	75	0	0	0	1	1	0.41	5.30		10
20	0	1	75	0	0	0	0	2	0.40	6.87		13
20	0	1	75	0	0	1	1	3	0.43	3.72		13
20	0	1	75	0	0	1	0	4	0.47	8.88		11
20	0	1	75	0	0	2	1	5	0.41	3.25		11
20	0	1	75	0	0	2	0	6	0.23	6.12	4	12
20	0	1	75	0	1	0	1	7	0.11	6.31		10
20	0	1	75	0	1	0	0	8	0.18	4.07		9
20	0	1	75	0	1	1	1	9	0.10	1.41		10
20	0	1	75	0	1	1	0	10	0.11	1.83		9
20	0	1	75	0	1	2	1	11	0.19	9.40		8
20	0	1	75	0	1	2	0	12	0.14	4.22	1	10
20	0	1	75	1	0	0	1	13	0.24	8.01		6
20	0	1	75	1	0	0	0	14	0.59	2.75		7
20	0	1	75	1	0	1	1	15	0.15	9.92		6
20	0	1	75	1	0	1	0	16	0.41	3.44		7
20	0	1	75	1	0	2	1	17	0.15	1.42		7
20	0	1	75	1	0	2	0	18	0.15	3.74	2	8
20	0	1	75	1	1	0	1	19	0.40	4.90		6
20	0	1	75	1	1	0	0	20	0.41	3.65		6
20	0	1	75	1	1	1	1	21	0.41	2.97		5
20	0	1	75	1	1	1	0	22	0.46	1.30		6
20	0	1	75	1	1	2	1	23	0.27	2.18		6
20	0	1	75	1	1	2	0	24	0.25	2.86	4	6
24	0	1	85	0	0	0	1	1	0.23	6.06		10
24	0	1	85	0	0	0	0	2	0.31	5.96		9
24	0	1	85	0	0	1	1	3	0.33	4.16		10
24	0	1	85	0	0	1	0	4	0.33	3.80		10
24	0	1	85	0	0	2	1	5	0.54	3.85		11
24	0	1	85	0	0	2	0	6	0.29	3.57	1	10
24	0	1	85	0	1	0	1	7	0.13	5.17		4
24	0	1	85	0	1	0	0	8	0.23	3.38		13
24	0	1	85	0	1	1	1	9	0.30	3.17		4
24	0	1	85	0	1	1	0	10	0.15	3.56		9
24	0	1	85	0	1	2	1	11	0.35	3.21		5
24	0	1	85	0	1	2	0	12	0.33	4.69	1	8
24	0	1	85	1	0	0	1	13	0.35	5.29		4

24	0	1	85	1	0	0	0	14	0.40	3.94		12
24	0	1	85	1	0	1	1	15	0.27	5.56		4
24	0	1	85	1	0	1	0	16	0.47	3.24		12
24	0	1	85	1	0	2	1	17	0.42	5.31		3
24	0	1	85	1	0	2	0	18	0.24	2.33	1	12
24	0	1	85	1	1	0	1	19	0.43	2.78		2
24	0	1	85	1	1	0	0	20	0.27	3.38		6
24	0	1	85	1	1	1	1	21	0.30	4.26		2
24	0	1	85	1	1	1	0	22	0.25	2.96		6
24	0	1	85	1	1	2	1	23	0.36	3.99		2
24	0	1	85	1	1	2	0	24	0.31	2.47	0	6

Appendix G – Eye analysis code

Files are in alphabetical order.

Batch_bed_anal.m

```
% Script modified by Cemocan S. Yesil, Summer 2003

close all
clear all

% set initial constants using the init_bed function -- Cemocan S. Yesil
[FALSE, TRUE, LEFT_VERTICAL, RIGHT_VERTICAL, LEFT_HORIZONTAL, RIGHT_HORIZONTAL,
num_increase, num_RMS, min_diff_class] = init_bed;

batch_mode = TRUE;

% get research data folder name
[master_path, data_path] = get_PC_bed_path;

% get list of patients to be processed
[code_length, patient_list] = get_patient_list(data_path, master_path);

[num_patients,n] = size(patient_list);

% Tell the user what is happening, added by IGB Sept 2003
fprintf(['\nData from each run will be stored in separate matlab files for each eye and axis.']);
fprintf(['\n']);

for patnum=1:num_patients,

        file_name = patient_list(patnum,:);
        idx = find(abs(file_name) > 32);                % printable non-blank characters
        file_name = file_name(idx);

        idx = find(file_name == '.');
        if (isempty(idx)),
                root_file = file_name;
        else
                root_file = file_name(1:(idx(1)-1));
        end

        % Convert the bed file into components usable by eye_anal_manual
  % and save variables in .mat files with the proper run and eye
  % extensions in the file name -- Cemocan S. Yesil
  [data, num_runs, root_file, num_samples, sample_rate, num_params] = convert_bed_file(data_path, file_name);

  for rn=1:num_runs,
        if (rn < 10),
                        run_code = [root_file, '_run0', int2str(rn)];
                else
                        run_code = [root_file, '_run', int2str(rn)];
        end
                run_file = [data_path, run_code, '.mat'];

                fprintf(['\nProcessing ', run_code, ' ...']);
```

```
                load(run_file);

                batch_bed_file(patient_list, run_code, master_path, data_path, data, LEFT_VERTICAL,
RIGHT_VERTICAL, LEFT_HORIZONTAL, RIGHT_HORIZONTAL, min_diff_class, num_RMS, num_increase,
TRUE, num_samples, sample_rate, num_params);

  end

end

fprintf(['\n\nProcessing complete. Use "eye_anal_manual" to analyze the data manually.']);
fprintf(['\n']);
```

batch_bed_file.m

```
% File modified and converted into a function by Cemocan S. Yesil, Summer
% 2003

function batch_bed_file(patient_list, run_code, master_path, data_path, data, LEFT_VERTICAL,
RIGHT_VERTICAL, LEFT_HORIZONTAL, RIGHT_HORIZONTAL, min_diff_class, num_RMS, num_increase,
TRUE, num_samples, sample_rate, num_params)

% create time vector
t = [0:(num_samples-1)] / sample_rate;

%
% process left vertical eye position data
%
raw_index = LEFT_VERTICAL;
cal_index = LEFT_VERTICAL+num_params;
which_eye = 'Left Vertical';
file_ext = '_LV.mat';

batch_eye_channel(patient_list, file_ext, run_code, master_path, data_path, data, raw_index, cal_index, num_increase,
sample_rate, TRUE, num_RMS, min_diff_class);

%
% process right vertical eye position data
%
raw_index = RIGHT_VERTICAL;
cal_index = RIGHT_VERTICAL+num_params;
which_eye = 'Right Vertical';
file_ext = '_RV.mat';

batch_eye_channel(patient_list, file_ext, run_code, master_path, data_path, data, raw_index, cal_index, num_increase,
sample_rate, TRUE, num_RMS, min_diff_class);

%
% process left horizontal eye position data
%
raw_index = LEFT_HORIZONTAL;
cal_index = LEFT_HORIZONTAL+num_params;
which_eye = 'Left Horizontal';
file_ext = '_LH.mat';

batch_eye_channel(patient_list, file_ext, run_code, master_path, data_path, data, raw_index, cal_index, num_increase,
sample_rate, TRUE, num_RMS, min_diff_class);

%
% process right horizontal eye position data
%
```

```
raw_index = RIGHT_HORIZONTAL;
cal_index = RIGHT_HORIZONTAL+num_params;
which_eye = 'Right Horizontal';
file_ext = '_RH.mat';

batch_eye_channel(patient_list, file_ext, run_code, master_path, data_path, data, raw_index, cal_index, num_increase,
sample_rate, TRUE, num_RMS, min_diff_class);
```

batch_eye_channel

```
% batch_eye_channel

% File modified and converted into a function by Cemocan S. Yesil, Summer
% 2003

function batch_eye_channel(patient_list, file_ext, run_code, master_path, data_path, data, raw_index, cal_index,
num_increase, sample_rate, TRUE, num_RMS, min_diff_class)

% free up variable space
clear pos vel spv edited_spv filt_spv fast_start fast_end

% detect blinks using raw data, but make interpolations on calibrated data
[pos, num_blinks, perc_blink] = deblink(data(:,raw_index), data(:,cal_index), 0, 0, num_increase);

% filter eye position data to enhance signal-to-noise ratio
%       - one pass of order statistic filter to minimize video quantization,
%               allowing for curved eye movements
%       - two passes of fourth-order phase-less Butterworth low-pass filter
%               with 30 Hz corner frequency, to reduce noise
%       - two additional passes of order statistic filter, to reduce noise
%               and sharpen corners of nystagmus, allowing for curved eye movements
pos = filt_position(pos, sample_rate, 2, 3, TRUE);

% differentiate eye position to get velocity
vel = differentiate(pos, sample_rate);

% classify fast phases in eye velocity data, and interpolate across
[fast_start, fast_end] = bed_classify_phases(vel, num_RMS, num_increase, ...

        min_diff_class, sample_rate);
spv = interpolate(vel, fast_start, fast_end);

% no manual editing in batch processing, so no edited_spv
edited_spv = [];

% save data in a Matlab-format file
save_file = [data_path, run_code, file_ext];
parms_list = ' pos vel spv edited_spv fast_start fast_end num_blinks perc_blink';
eval(['save ', save_file, parms_list]);
```

bed_classify_phases.m

```
function [fast_start, fast_end] = bed_classify_phases(vel, num_RMS, ...
                                                                num_increase,
min_diff_class, sample)
%
% bed_classify_phases.m  - attempts to detect fast phases in a velocity trace 'vel'
%
% The velocity data is filtered by the AATM algorithm, to calculate an estimate
```

```
%       of SPV. The difference between the raw eye velocity and the AATM velocity
%       is calculated. Any difference which exceeds a specified multiple (num_RMS)
%       of the RMS difference, and which also exceeds a specified absolute threshold
%       (min_diff_class), is classified as a "fast" point. A fast phase is defined
%       as a series of consecutive fast points. A specified number of points
%       (num_increase) are added to the beginning and end of the fast phase, to allow
%       for transient behaviour, particularly due to digital filtering effects.
%       "fast_start" is a vector in which each element is the sample number of the
%       start of a fast phase. "fast_end" contains the corresponding sample
%       numbers of the ends of the fast phases.
%
% Note: fast phases in the first or last half-second of data will not be properly detected
%
% Suggested values for the input parameters are:
%       vel = eye velocity, calculated by differentiating calibrated eye position
%       num_RMS = 0.25
%       num_increase = 2
%       min_diff_class = 30
%       sample = 60
%
% Written by: MDB 10/1/99
%

last = length(vel);
AATM_transient = num_increase;

% run AATM filter over data
AATM_spv = newAATM(sample+1, vel);                    % one second filter window

% find data points for which velocity and AATM are within 'num_RMS'
i = 1 + AATM_transient;
j = last - AATM_transient;
slow = min_threshold( vel(i:j), AATM_spv(i:j), num_RMS, min_diff_class );
slow = [zeros(AATM_transient,1) ; slow ; zeros(AATM_transient,1)];
fast = ~slow;
clear i j AATM_transient

% increase fast phase duration by 'num_increase' sample
%   in each direction for transients
if (num_increase > 0),
   fast = filtfilt(ones(num_increase+1,1), 1, fast);
   fast = (fast > 0);
end

% find start and end of each fast phase
fast_diff = filter([1 -1], 1, fast);   % two-point difference
fast_start = find(fast_diff > 0);                    % 0 to 1 transition
num_start = length(fast_start);
fast_end = find(fast_diff < 0) - 1;                          % 1 to 0 transition
num_end = length(fast_end);
if (num_end < num_start),
   fast_end = [fast_end; last];
   num_end = num_end + 1;
end

clear slow fast num_slow fast_diff num_end num_start
```

check_curve.m

```
%function ftest = checkcurve(spv, startPt, a_check, tau_check, num_pts)
```

```
function ftest = checkcurve(modspv, a_check, tau_check)
% Checks curve goodness of fit using F-test
% requires spv, startPt, A, tau, number of points
% By David Phillips, March 28, 2001
%   SSQT = Total Sum of Squares (fitted-avg)
%   SSQE = Error Sum of Squares (point-fitted)
%   SSQR = Regress Sum of Squares (SSQT-SSQE)
% Modified by Ian Garrick-Bethell, March 08, 2004
% Modified to allow fewer inputs, and just an array of data can be entered.

clear t;
%t=rot90([1:num_pts+1]/60,-1); % t=time in sec
t = [1:length(modspv)]'/60;
%modspv=spv(startPt:startPt+num_pts);            % modspv is spv for num_pts

curve_vals=a_check*exp(-t/tau_check);

avgspv = mean(modspv(:,2));
size(avgspv)
SSQT = sum((modspv(:,2)-avgspv).^2);
SSQE = sum((modspv(:,2)-curve_vals).^2);
SSQR = SSQT - SSQE;

%ftest=(SSQR/2)/(SSQE/num_pts-3); % 2 degrees of freedom for A, tau, 3 for A, tau, mean
ftest=(SSQR/2)/(SSQE/length(modspv)-3); % 2 degrees of freedom for A, tau, 3 for A, tau, mean

% compare f-test to 3.00 for 2DOF (A, tau), P=0.05, infinite points (~=600pts)
```

convert_bed_file.m

```
% File modified and converted into a function by Cemocan S. Yesil, Summer
% 2003

function [data, num_runs, root_file, num_samples, sample_rate, num_params] = convert_bed_file(data_path,
file_name)

fid = fopen([data_path,file_name],'r');

%
% decipher header information
%

% Sometimes, header info is tab-delimited
% In other cases, it is separated by blank spaces
% In either situation, looking for unprintable characters seems to work,
%   to find either tab (9) or carriage return (13).

TAB = 9; % tab character seems to be used in header info, instead of blank space
COLON = 58;
BLANK = 32;

iscan_ver = fgets(fid);                    % ISCAN version number, and file format

% discard two lines
inline = fgets(fid);
inline = fgets(fid);

% subject name
inline = fgets(fid);
l = length(inline);
cl = find(abs(inline) == COLON);           % look for ":" in string
```

```
str = inline( (cl(1)+1) : l );
tb = find(abs(str) < BLANK);            % look for "tab" or "cr" in sub-string
subject_name = str( (tb(1)+1) : (tb(2)-1) );

% test date
inline = fgets(fid);
l = length(inline);
cl = find(abs(inline) == COLON);                % look for ":" in string
str = inline( (cl(1)+1) : l );
tb = find(abs(str) < BLANK);            % look for "tab" or "cr" in sub-string
test_date = str( (tb(1)+1) : (tb(2)-1) );

% test description
inline = fgets(fid);
tb = find(abs(inline) == COLON);                % look for "colon" in string
l = length(inline);
if (inline(tb(1)+1) <= BLANK),
        test_descr = inline( (tb(1)+2) : (l-1) );
else
        test_descr = inline( (tb(1)+1) : (l-1) );
end

% discard line
inline = fgets(fid);

% number of runs
inline = fgets(fid);
l = length(inline);
cl = find(abs(inline) == COLON);                % look for ":" in string
str = inline( (cl(1)+2) : l );
tb = find(abs(str) < BLANK);            % look for "tab" or "cr" in sub-string
num_runs = eval( str(1:(tb(1)-1)) );

% total number of points recorded (i.e. number of samples)
inline = fgets(fid);
l = length(inline);
cl = find(abs(inline) == COLON);                % look for ":" in string
str = inline( (cl(1)+2) : l );
tb = find(abs(str) < BLANK);            % look for tab or "cr" in sub-string
total_pts = eval( str(1:(tb(1)-1)) );

% total number of parameters recorded (i.e. number of raw data channels)
inline = fgets(fid);
l = length(inline);
cl = find(abs(inline) == COLON);                % look for ":" in string
str = inline( (cl(1)+2) : l );
tb = find(abs(str) < BLANK);            % look for tab/cr in sub-string
num_params = eval( str(1:(tb(1)-1)) );

% discard three lines
inline = fgets(fid);
inline = fgets(fid);
inline = fgets(fid);

% parse out number of points in each run
run_points = zeros(num_runs,1);                 % number of samples in each run
run_rate = zeros(num_runs,1);                   % sampling rate for each run
run_start = [];                 % start time for each run
for i=1:num_runs,
        inline = fgets(fid);
        l = length(inline);
        tb = find(abs(inline) == TAB);                  % look for "tab" in string
```

```
        if (inline(l-1) >= BLANK),
                tb = [0, tb, l];
        end
        run_points(i) = eval( inline( (tb(1)+1) : (tb(2)-1) ) );
        run_rate(i) =  60; %eval( inline( (tb(2)+1) : (tb(3)-1) ) );  %SAMPLING RATE
        run_start = [run_start; inline( (tb(3)+1) : (tb(3)+9) )];
end

% discard three lines
inline = fgets(fid);
inline = fgets(fid);
inline = fgets(fid);

% parse information for names of channels, and mean and standard deviation
%   of each channel over length of runs
param_name = [];
name_len = 10;                  % allow parameter names up to 10 characters long
all_raw_mean = zeros(num_params,num_runs);
all_raw_std = zeros(num_params,num_runs);
all_cal_mean = zeros(num_params,num_runs);
all_cal_std = zeros(num_params,num_runs);
for i=1:num_params,

        % extract name of parameter
        inline = fgets(fid);
        idx = find(inline == '(');                      % look for "(" in string
        pn = inline(2: (idx(1)-2));
        l = length(pn);
        if (l < name_len),    % pad with blanks
                pn = [pn, blanks(name_len - l)];
        else        % truncate length
                pn = pn(1:name_len);
        end
        idx = find(pn < BLANK);
        for k=1:length(idx),            % replace tabs with blank characters
                pn(idx(k)) = BLANK;
        end
        param_name = [param_name; pn];

        % extract mean of raw data from same line
        idx = find(inline == ')');                      % look for ")" in string
        str = inline( (idx(2)+1) : length(inline) );
        idx = find(abs(str) < BLANK);                           % look for non-numeric in sub-string
        for j=1:num_runs,
                num = eval(str( (idx(j)+1) : (idx(j+1)-1) ));
                all_raw_mean(i,j) = num;
        end

        % extract standard deviation of raw data
        inline = fgets(fid);
        idx = find(inline == ')');                      % look for ")" in string
        str = inline( (idx(2)+1) : length(inline) );
        idx = find(abs(str) < BLANK);                           % look for non-numeric in sub-string
        for j=1:num_runs,
                num = eval(str( (idx(j)+1) : (idx(j+1)-1) ));
                all_raw_std(i,j) = num;
        end

        % extract mean of calibrated data
        inline = fgets(fid);
        idx = find(inline == ')');                      % look for ")" in string
        str = inline( (idx(2)+1) : length(inline) );
```

```
        idx = find(abs(str) < BLANK);                   % look for non-numeric in sub-string
        for j=1:num_runs,
                num = eval(str( (idx(j)+1) : (idx(j+1)-1) ));
                all_cal_mean(i,j) = num;
        end

        % extract standard deviation of calibrated data
        inline = fgets(fid);
        idx = find(inline == ')');                      % look for ")" in string
        str = inline( (idx(2)+1) : length(inline) );
        idx = find(abs(str) < BLANK);                   % look for non-numeric in sub-string
        for j=1:num_runs,
                num = eval(str( (idx(j)+1) : (idx(j+1)-1) ));
                all_cal_std(i,j) = num;
        end

end

% discard three lines
inline = fgets(fid);
inline = fgets(fid);
inline = fgets(fid);
inline = fgets(fid);

num_channels = 2*num_params + 1;    % raw and calibrated, plus sample number

idx = find(file_name == '.');
if (isempty(idx)),
        root_file = file_name;
else
        root_file = file_name(1:(idx(1)-1));
end

% Tell user what's happening - Added by IGB, Sept 2003
disp('Now converting ISCAN ASCII data file into Matlab workspace files.');

for i=1:num_runs,

        % input data for run
        num_samples = run_points(i);

        fprintf(['\nConverting ', file_name, ' -- run #', int2str(i), ' (', ...
                        int2str(num_samples), ' samples) ...']);

        clear data
        data = zeros(num_samples, num_channels);

        for j=1:num_samples,

if (~rem(j,1000)),
        fprintf('\n  finished %d', j);
end

                inline = fgets(fid);
                idx = find(abs(inline) < BLANK);        % look for non-numeric in string
                if (idx(1) > 2),
                        idx = [1,2,idx];
    elseif (idx(2) > 2),
      idx = [1,idx];
    end

    for k=1:num_channels,
```

```
                        num = eval(inline( (idx(k+1)+1) : (idx(k+2)-1) ));
    data(j,k) = num;
   end
  end

        % save data for this run in a separate mat-file
        sample_rate = 60; %run_rate(i);
        start_time = run_start(i,:);
        raw_mean = all_raw_mean(:,i);
        raw_std = all_raw_std(:,i);
        cal_mean = all_cal_mean(:,i);
        cal_std = all_cal_std(:,i);

  % name the files
        if (i < 10),
   out_file = [data_path, root_file, '_run0', int2str(i), '.mat'];
        else
                out_file = [data_path, root_file, '_run', int2str(i), '.mat'];
  end

  % save variables to be used by eye_anal_manual in data processing --
  % Cemocan S. Yesil
  param_list = 'data iscan_ver subject_name test_date test_descr num_runs';
        param_list = [param_list, ' total_pts num_params num_samples sample_rate'];
        param_list = [param_list, ' start_time raw_mean raw_std cal_mean cal_std'];
        param_list = [param_list, ' param_name num_channels out_file'];

  eval(['save ', out_file, ' ', param_list]);

        % discard one line
        inline = fgets(fid);

end

fprintf('\n');

fclose(fid);
```

data_eliminator.m

```
function [new_data] = data_eliminator(the_data)

% Written by Ian Garrick-Bethell, email: iang@mit.edu
% THIS IS A BETA VERSION
% This function takes an array of data (the_data) as an n x 2 array, with y values first, then x values,
% and allows the user to draw a shape around unwanted data.
% The unwanted data is then eliminated, and the edited data is passed out as
% "new_data", with x-y relations preserved. That is, the specific x-y
% pairing are kept the same. No concatenation takes place.
% The technique involves creating a shape from a set of lines that the
% user enters with the mouse.
% Points inside the shape to be eliminated are determined by "drawing" infinite horiztonal
% lines through all points in the the array 'the_data'.
% Then, these horizontal lines are checked for the number of intersections
% with the shape edges. If the number of intersections on the left or
% right of the data point is odd, then the point is inside the shape, and it is eliminated.
% If the number of intersections on the left or right of the data point is even, or zero,
% then the point is outside the shape, and it is kept.
% Suggest using 4-8 sided shapes, preferably without vertical or horizontal edges.
% NOTE: this version does not correct for vertical lines with cause an error.
warning off MATLAB:divideByZero % Turn off this warning, it shouldn't matter. Has to do w/ slopes of 0
```

```
[xx, yy] = ginput;
  % % Accomodate the difference between the axis the data is plotted on, and
  % % the true x axis values that are associated with the data
  % xx = xx/graph_scale;
  % yy = yy/graph_scale;

% Check if the user picked one or no points, implying they don't want to do anything
if length(xx) <= 2
   new_data = the_data;
   disp('***All data is being kept***');
   return % Return control to the function that called us
end

%-----------------------------------------------------------------
% Define the user inputed shape as a set of lines, and plot them
%-----------------------------------------------------------------

% Create an array of line equations that correspond to the points selected.
% Format: n x 2: [m b], for y = mx + b (m is slope, b is y intercept).
for k = 1:(length(xx)-1)
% First calculate m:
  m = (yy(k+1) - yy(k))/(xx(k+1) - xx(k));
  % Now calculate b:
  b = yy(k) - m*xx(k);
  % Write the line equation into the array:
  the_lines(k,1) = m;
  the_lines(k,2) = b;
end

% Now add in the eq. of the line that connects the first point to the last point:
m_final = (yy(length(xx)) - yy(1))/(xx(length(xx)) - xx(1));
b_final = yy(length(xx)) - m_final*xx(length(xx));
the_lines(length(xx),1) = m_final;
the_lines(length(xx),2) = b_final;

% Plot the array of lines
figure(1), hold on;
plot(xx, yy, '*');
for q = 1:length(the_lines)
 % First create a string that describes the function:
 function_string  = [num2str(the_lines(q,1)) '*x + ' num2str(the_lines(q,2))];
 % Now plot these linse over the appropriate ranges
 if q ~= length(the_lines) % Are we at the end of the line array, where the last line is connected to the first?
  value_1 = xx(q);
  value_2 = xx(q+1);
 else
  value_1 = xx(q);
  value_2 = xx(1);
 end
 if value_1 < value_2 % What are the limits, depending on the x values of the two endpoints?
  ezplot(function_string, [value_1, value_2]);
 elseif value_1 > value_2
  ezplot(function_string, [value_2, value_1]);
 else % They are equal
  ezplot(function_string, [-5,20]);
  error('hi');
 end
 %axis([-5, 20, -60, 60]);
 axis([the_data(1,1),the_data(length(the_data),1), 1.1*min(the_data(:,2)), 1.1*max(the_data(:,2))]);
 %plot(xx, yy, 'k*');
 % pause;
```

```
end

%------------------------------------------------------------------------
% Determine which points from the_data are inside the user defined shape
% This starts a major loop.
%------------------------------------------------------------------------

tic;
c = 1; % Initialize counter for the new_data array
for w = 1:length(the_data)
   % Create the horizontal line associated with the point for plotting,
   % if desired
   eval_function_string  = [num2str(the_data(w,2))];

  z = 1;
  side_counter = 0;
  % Determine all intersection points btwn the point's horz line and shape lines
  % METHOD: backwards solve the equations: (y - b) / m = x
  clear common_x_value;
  clear relevant_x_values;
  for r = 1:length(the_lines)
     % common_x_value is the intersection x value for the horz. line and ALL shape lines
     common_x_value(r) = (the_data(w,2) - the_lines(r,2))/the_lines(r,1);
     % plot(common_x_value, eval_pointy, 'g+');

    % Determine which of the relevant intersection points (those that are on the shape
    % edge that is cross-cut by the horizontal line that describes the chosen point)
    % CRITERIA: if the 2 endpoints points making up the shape edge are above
    % AND below the data point, then that data point's horizontal line intersection
    % is at the true edge of the shape.
    % Note that other horz. line-edge intersections will be formed from lines that
    % are not locally relevant (do not truly describe the shape at the
    % intersection) and intersect further away from the shape.
    % Here "reveleant x values" are defined as data points that are vertically between
    % intersections of user selected shape verticies (satisfy above criteria).
    % The_data(x,2) represents y values and the_data(x,1) represents x values

    if r ~= length(the_lines) % Make sure you check the first and last horiz. line separately
     if ((yy(r+1) <= the_data(w,2)) & (the_data(w,2) <= yy(r))) |...
          ((yy(r) <= the_data(w,2)) & (the_data(w,2) <= yy(r+1))) % Check vert. inbetweenness
       % Create matrix with values and a left/rightness indicator in 2nd column
       relevant_x_values(z,1) = common_x_value(r);
       if relevant_x_values(z,1) < the_data(w,1) % is it to the left of the edge?
         relevant_x_values(z,2) = 0; % gets a zero for left
         side_counter = side_counter + 1;
       elseif relevant_x_values(z,1) > the_data(w,1) % is it to the right of the edge?
         relevant_x_values(z,2) = 1; % gets a 1 for right
         side_counter = side_counter + 1;
       else
         disp('POINT IS ON EDGE!!!!!!!!!!');  %(relevant_x_val. = data val.)
         the_data(w,1)
%           break; % break out of the loop, since the point is considered in the figure
%           side_counter = side_counter + 1;
       end
       z = z + 1;
     end

    else % For the last line
     if ((yy(r) <= the_data(w,2)) & (the_data(w,2) <= yy(1))) |...
          ((yy(1) <= the_data(w,2)) & (the_data(w,2) <= yy(r))) % Check vert. inbetweenness
       % Create matrix with values and a left/rightness indicator in 2nd column
       relevant_x_values(z,1) = common_x_value(r);
```

```
    if relevant_x_values(z,1) < the_data(w,1) % is it to the left of the edge?
      relevant_x_values(z,2) = 0;  % gets a zero for left
      side_counter = side_counter + 1;
    elseif relevant_x_values(z,1) > the_data(w,1) % is it to the right of the edge?
      relevant_x_values(z,2) = 1; % gets a 1 for right
      side_counter = side_counter + 1;
    else
     disp('POINT IS ON EDGE!!!!!!!!!!');
     the_data(w,1);
    end
    z = z + 1;
   end

 end

end % This is the end of the line loop for each data point

% ****************************************************************
% Populate a new array with the values OUTSIDE of the user's figure
% (we're still in the largest loop)
%*****************************************************************
if z == 1 %Point is exterior to shape because point was not vertically
       %in between any verticies
 new_data(c,1) = the_data(w,1);
 new_data(c,2) = the_data(w,2);
 c = c + 1;  % increment the new_data counter
 %disp('no vertical inbetweenness');
 continue; % skip to the next data loop iteration, since we know the point is outside.
 % note that this also avoids referencing the now undefined variable
 % relevant_x_values
end

% Now, for points that are vertically between verticies, determine if the
% point is inside or out based on the number of edges on the right and left.
% INSIDE THE FIGURE: odd number of edges to the left and right
% OUTSIDE THE FIGURE: even number of edges to the left and right
left_right_sum = sum(relevant_x_values, 1); % Sum up the values of left and rightness edges markers
left_right_score = left_right_sum(2);      % Is this even or odd?

if mod(left_right_score,2) == 0      % This is an even number of edges to both left/right of data
  new_data(c,1) = the_data(w,1);
  new_data(c,2) = the_data(w,2);
  c = c + 1;                    % increment the new_data counter
  %disp('Point is outside of the object');
elseif mod(left_right_score,2) == 1  % Odd number of edges to L & R (could use just 'else')
  % No new data is written to new_data, and the "c" counter value
  % remains the same
  % disp('Point is inside of the object');
end
%*****************************************************************

end % ***** This is the end of the main loop over the data array *****
toc;

% figure(333);
% plot(new_data(:,1),new_data(:,2), '.');

the_data_size = size(the_data);
new_data_size = size(new_data);
points_removed = the_data_size(1) - new_data_size(1);
disp(['A total of ', int2str(points_removed), ' points were removed.']);
```

```
warning on MATLAB:divideByZero % Turn the warning back on
```

deblink.m

```
function [y, num_blinks, perc_blink] = deblink(x, xcal, low, high, num_increase)

% detects blinks on position trace "x" using threshold "thresh".
%  low > 0  ==>  use the specified values, call "thresh_blinks"
%  low = 0  ==>  rely on ISCAN zeros for blinks, call "simple_blinks"
%  low < 0  ==>  calculate thresholds based on mean and standard deviation
%                                        and iterate with operator control, call "thresh_blinks"
% "xcal" is calibrated position, while "x" is raw data
%        detect blinks using "x", but make interpolations on "xcal"
%        if "xcal" is empty, assume "x" is calibrated data
% "y" is eye position data with blinks removed by linear interpolation
% "num_blinks" is the number of blinks which were detected in the trace
% "perc_blink" is the percentage of the trace which is defined as a blink
%

if (low == 0),

        [s,e] = simple_blinks(x, num_increase, 100);

elseif (low > 0),

        [s,e] = thresh_blinks(x, num_increase, low, high, 100);

else

        mn = mean(x);
        sd = std(x);
        low = mn - 3*sd;
        if (low < 0),
                low = 0;
        elseif (low > 500),
                low = 500;
        end
        high = mn + 3*sd;
        if (high < 3500),
                high = 3500;
        elseif (high > 4000),
                high = 4000;
        end

        [s,e] = thresh_blinks(x, num_increase, low, high, 100);
        x2 = interp_blinks( x, s, e);
        fig = figure('Name', 'Specification of Blink Threshold');
        h1 = plot(x, 'y');
        hold on
        h2 = plot(x2, 'b');
        xl = get(gca,'XLim');
        h3 = plot(xl, [low low], 'g');
        h4 = plot(xl, [high high], 'r');

        low2 = input('Specify new value for low threshold (-1 to end): ');
        if (isempty(low2)),
                low2 = 0;
        else
                if (low2 >= 0),
                        low = low2;
                end
```

```
        end
        high2 = input('Specify new value for high threshold (-1 to end): ');
        if (isempty(high2)),
                high2 = 0;
        else
                if (high2 >= 0),
                        high = high2;
                end
        end

        while ((low2 >= 0) | (high2 >= 0)),

                [s,e] = thresh_blinks(x, num_increase, low, high, 100);
                x2 = interp_blinks( x, s, e);
                set(h2, 'YData', x2);
                set(h3, 'YData', [low low]);
                set(h4, 'YData', [high high]);

                low2 = input('Specify new value for low threshold (-1 to end): ');
                if (isempty(low2)),
                        low2 = 0;
                else
                        if (low2 >= 0),
                                low = low2;
                        end
                end
                high2 = input('Specify new value for high threshold (-1 to end): ');
                if (isempty(high2)),
                        high2 = 0;
                else
                        if (high2 >= 0),
                                high = high2;
                        end
                end

        end

        delete(h4);
        delete(h3);
        delete(h2);
        delete(h1);
        close(fig);
        clear x2

end

if (isempty(xcal)),
        y = interp_blinks( x, s, e);
else
        y = interp_blinks( xcal, s, e);
end

num_blinks = length(s);
if (num_blinks > 40),
        fprintf('\n    WARNING: dangerously high blink activity (%d blinks)', num_blinks);
end
perc_blink = 100 * (sum(e - s - 1) / length(x));
if (perc_blink > 3),
        fprintf(['\n    WARNING: dangerously high blink activity (%5.2f%c)'], perc_blink,37);
end
```

```
return;
```

differentiate.m

```
function xprime = differentiate( x, sample )

% differentiate - returns the first time derivative of 'x'
%
% Written by: D. Balkwill 10/20/93
%

A = 1 / sample;
if (sample == 60),
        B = [0.0077, 0.0714, 0.1078, 0.0870, 0, -0.0870, -0.1078, -0.0714, -0.0077];
else
        B = [0.0332, 0.0715, 0.0678, 0.0522, 0, -0.0522, -0.0678, -0.0715, -0.0332];

end
gain = [4 3 2 1] * B(1:4)' * 2;
B = B / gain;
xprime = zero_filter(B, A, x);

clear A B gain
```

exp_fit.m

```
function [a_temp, tau_temp] = dave_expfit(data)
% Function [a_temp, tau_temp] = dave_expfit(start_ind,spv,num_pts)
% Written by Dave
% Modified by Ian Garrick-Bethell
% For a meaningful result, ensure that the data is in units of time, not k (samples).
% Note that the start time must be zero seconds
%for startPt = 1:50:1000,
  %x =  [1:(num_pts+1)]' / 60;            % x=time (in secs)
  %data = [x, spv(start_ind:start_ind+num_pts)];  % data = [time(in secs), spv]

  % shift the x data to start at t = 0 for the curve fitting
  %data(:,1) = [1:length(data)]' / 60;

  % Perform the curve fit
  startParams = [10, 20];
  options = optimset('Display', 'off');
  bestFitVals = FMINSEARCH('expCost', startParams, options, data);
  tau_temp = bestFitVals(1);
  a_temp = bestFitVals(2);
%end
```

expCost.m

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
function cost = expCost(params, data)

tau_temp = params(1);
a_temp = params(2);

curveVals = a_temp * exp(-data(:, 1) / tau_temp);
cost = sum((data(:, 2) - curveVals) .^ 2);  % sum of least mean squares
```

eye_anal_manual.m

```
% This script analyzes the eye & button data using a manual click
% as the trigger for start of nystagmus. Outputs to screen.
% By: David Phillips March 28, 2001

% Script modified by Cemocan S. Yesil, Summer 2003
% Modified by Ian Garrick-Bethell, March 08, 2004

close all;
clear all;

% Allows user to modify the time span in seconds of the zoomed window
% modified by Ethan Post 7/3/03
zoom_time = 30;  %in seconds
zoom_samp = zoom_time * 60; % in samples;

% Read initial variables including raw data column numbers corresponding to
% different eyes and axes off of init_bed.m -- Cemocan S. Yesil
[FALSE, TRUE, LEFT_VERTICAL, RIGHT_VERTICAL, LEFT_HORIZONTAL, RIGHT_HORIZONTAL,
num_increase, num_RMS, min_diff_class] = init_bed;

batch_mode = FALSE;

load bed_path.mat;
% Commented out the load 'patient_list.mat' call so that the user can confirm the file being edited with
% Eye anal manual.  If the user is certain that the file is always the same, comment out the
% call to get_patient_list, and uncomment the load patient_list.mat (the workspace w/ the info)
% Modified by Ian Garrick-Bethell, Sept 16, 2003
% load patient_list.mat;
[code_length, patient_list] = get_patient_list(data_path, master_path);

[num_patients,n] = size(patient_list);
for patnum = 1:num_patients
  % Load .mat files with the appropriate run and eye extensions saved by
  % the script 'batch_bed_anal.m' -- Cemocan S. Yesil
  [run_code, eyeext] = load_file(data_path, patient_list, patnum);
  load([data_path, run_code, '.mat']);
  load([data_path, run_code, eyeext, '.mat']);

  Button = data(:,6); % Here, the button data is in 6th column

  x_length = max(length(spv),length(Button));
  % Graph full length of run
  clf;
  figure(1), hold off;
%   subplot(2,1,1)
  x = [1:x_length];
  %x_time = x/60;
   plot(x,spv)
     % Labels
   XaxisLabel = 'Samples';
   YaxisLabel = 'Slow phase velocity (degrees/second)';
   XLabel(XaxisLabel, 'FontSize', 8, 'FontWeight', 'bold');
   YLabel(YaxisLabel, 'FontSize', 8, 'FontWeight', 'bold');

%   subplot(2,1,2)
%   plot(x,Button)
pause;
```

```
% Ask user to select starting point to zoom in on
fprintf('\nClick on SPV start to zoom in.\n\n')
[zm,y] = ginput(1);
zm = round(zm); % in seconds

% Check if the zoomed region will exceed matrix dimensions
% Also, put the zoomed data into a separate array for future
% manipulation
%if (zm + zoom_time)*60 < length(spv)
if (zm + zoom_samp) < length(spv)
  % Note that the x value array is now inverted
  %zoomed_data = [x_time((zm-1)*60:(zm + zoom_time)*60)', spv((zm-1)*60: (zm + zoom_time)*60)];
   left = x(zm - 60);
   right = x(zm + (zoom_samp));
   top = 1.1 * max(spv((zm-60): zm + (zoom_samp)));
   bot = 1.1 * min(spv((zm-60): zm + (zoom_samp)));
   %zoomed_data = [zm-60:zm+ (60*zoom_time), spv(zm-60): zm + (60*zoom_time)]; % in samples now
else %it is too big
  left = x(zm - 60);
  right = x(length(spv));
  top = 1.1 * max(spv(zm-60:length(spv)));
  bot = 1.1 * min(spv(zm-60:length(spv)));
  % Note that the x value array is now inverted
  %zoomed_data = [x_time((zm-1)*60: length(spv))', spv((zm-1)*60: length(spv))];
end

% Now graph the zoomed data (from -1sec to +zoom_time seconds)
clf;
figure(1), hold off;
subplot(2,1,1);
 plot(x,spv, '.');
 axis([left, right, bot, top]);
%   axis([zm-1,zm + zoom_time,bot,top]);
%      plot(zoomed_data(:,2), '.');
%      axis([0,length(zoomed_data),bot,top]);

% Plot the zoomed button data
subplot(2,1,2);
plot(x,Button)
axis([left, right, 1000, 4000]);
%axis([zm-1,zm+15,1000,4000]);

over = 10;   % Used in the while loop for the curve endpoint selection

   %-------------------------------------------------------
    % Here the user manually inputs endpoint values for the
    % edited_data curve fit
   %-------------------------------------------------------
    while(over ~= 0)
      fprintf('Select start index by clicking: ');
      [start_click, y] = ginput(1);
      start_click = round(start_click); %in samples
      fprintf('%6.0f\n', start_click);
      fprintf('Select end index by clicking');
      [end_click, y] = ginput(1);
      end_click = round(end_click) %in samples
      fprintf('%6.0f\n\n', end_click);
      yn = get_yn('Accept these values?','Y');y
      if (yn == 'Y'),
       over = 0;
      end
   end
```

```
        % This part finds the point of local max of eye data between two mouse points,
        % then it finds the exponential curve & cumulative eye mvmt given that start index.
        % Find start of eye movement
        peak = spv(start_click);

        start_ind = start_click;
        num_pts = end_click - start_ind
        end_index = end_click;              % end of fit
       %-------------------------------------------------------
        cropped_data = [x(start_ind:start_ind + num_pts)', spv(start_ind:start_ind + num_pts)];

    %-------------------------------------------------------------------
    % Offer the user the option to eliminate noise and fit a curve to the
    % resultanting data
    %-------------------------------------------------------------------
     stop_editing = 0;
     while(stop_editing == 0)
        figure(1), subplot(2,1,1), hold on;
        plot(cropped_data(:,1), cropped_data(:,2), '.');
        axis([cropped_data(1,1), cropped_data(length(cropped_data),1), bot, top]);

        disp('Select a simple region of data to eliminate, or press ENTER to continue.');
        edited_data = data_eliminator(cropped_data); % feed in the zoomed_data array
        %Plot the edited data in samples (not time)
        figure(1), subplot(2,1,2);
%         plot(edited_data(:,1), edited_data(:,2), '.');
%         axis([zm-1,zm + zoom_time,bot,top]);
        plot(edited_data(:,1), edited_data(:,2), '.');
        axis([cropped_data(1,1), cropped_data(length(cropped_data),1), bot, top]);
        cropped_data = edited_data;
        yn_edit = get_yn('Are you finished removing data?','Y');
         if (yn_edit == 'Y')
           stop_editing = 1;
         end
      end
%
%         %Prepare the data for the exponential fit (THIS WOULD BE W/O
%         %EDITING
%         %the_data = [x_time(start_ind:start_ind + num_pts)', spv(start_ind:start_ind + num_pts)];
%
%         % Prepare the edited data for the exponential fit
% %           test = edited_data(start_ind:start_ind + num_pts - 1,2);
% %           length(test)
% %           test2 = [1:num_pts]' / 60;
% %           length(test2)
%         start_time = start_ind;
%         % subtract from each time in edited_data the the start_time, so
%         % that edited_data is reset to start at t = 0, which is required
%         % for the exponential fit
        the_data = [(edited_data(:,1) - start_ind)/60, edited_data(:,2)];


        %*******************************************************
        % NOTE THAT THE DATA MUST KEEP ITS X-Y ASSOCIATIONS!!!!
        %*******************************************************

        %Fit the curve
        [A_temp, tau_temp] = exp_fit(the_data);  % DATA MUST BE IN SECONDS AND START AT t = ZERO
        % Append A_temp, tau_temp to A, tau vectors
        A = A_temp;
        tau = tau_temp;
```

```
    % curve fit goodness
    ftest = checkcurve(the_data, A, tau);
  %-------------------------------------------------------------------
  %-------------------------------------------------------------------

  %------------------cumulative spv--------------------
  % This uses spv, not the fitted A, tau curve.
    end_eye = 10;   % for 10sec
    t_matrix = transpose(0:.01:10);
    curve = A*exp(-t_matrix/tau);
    cum_eye = trapz(t_matrix,curve);

 start_time = start_click/60;          % Printed as Clk_Start
 click_dur = end_click/60 - start_time; % Printed as Click_Dur

%  Creates text files, before attempting to edit them - CSY, 03/07/03
%  write_file = [data_path, run_code, eyeext, '_results.txt'];
%  fid = fopen(write_file, 'w');
%  fprintf(fid, '\nClk_Start\tClick_Dur\t Eye_Start\t  || A\t    Tau\t Cum_Eye\t  F-Test\n');
%  fprintf(fid, ' %8.4f\t %8.4f\t\t %6.0f\t %8.4f\t %8.4f\t %8.4f\t %8.4f\n'...
%           , start_time, click_dur, start_ind, A, tau, cum_eye, ftest);
%  fclose(fid);

%  % -----Open file to be displayed with the option of editing--------
%  % ----------OPTIONAL----------------
%  %  edit_file=[data_path, run_code, eyeext, '_results.txt'];
%  %  edit(edit_file);

 % Write to screen
 fprintf('\nClk_Start\tClick_Dur\t Eye_Start\t  || A\t    Tau\t Cum_Eye\t  F-Test\n');
 fprintf(' %8.4f\t %8.4f\t\t %6.0f\t %8.4f\t %8.4f\t %8.4f\t %8.4f\n'...
        , start_time, click_dur, start_ind, A, tau, cum_eye, ftest);

  %-------------------------------------------------------------
  % Plot fitted line
  %-------------------------------------------------------------
  time = rot90([1:num_pts+1]/60,-1);
  curveVals = A * exp(-time / tau);
  axismin = min(spv(start_ind:start_ind+num_pts))-5;
  axismax = max(spv(start_ind:start_ind+num_pts))+5;

  %clf, hold on,
  figure(2), hold on;
%   subplot(2,1,1);
%   % plot the data
%   plot(time, spv(start_ind:start_ind+num_pts),...
%     'o',...
%     'MarkerSize', 2,...
%     'MarkerFaceColor', 'b',...
%     'MarkerEdgeColor', 'b'...
%     );
%   axis([0,time(end),axismin,axismax]);
%
%   % plot the fitted curve
%   subplot(2,1,1), hold on;
%   plot(time, curveVals,...
%     'LineStyle', '-',...
%     'Color', 'k',...
%     'LineWidth', 1);
%
%   axis([0,time(end),axismin,axismax]);
```

```
%
%    % Labels
%    XaxisLabel = 'Time (seconds)';
%    YaxisLabel = 'SPV (degrees/second)';
%    XLabel(XaxisLabel, 'FontSize', 8, 'FontWeight', 'bold');
%    YLabel(YaxisLabel, 'FontSize', 8, 'FontWeight', 'bold');

   % plot the edited data
%    subplot(2,1,2)
    plot(the_data(:,1), the_data(:,2),...
      'o',...
      'MarkerSize', 2,...
      'MarkerFaceColor', 'b',...
      'MarkerEdgeColor', 'b'...
      );
   %axis([0,time(end),axismin,axismax]);

   % plot the fitted curve over the edited data
%    subplot(2,1,2), hold on;
   plot(time, curveVals,...
     'LineStyle', '-',...
     'Color', 'k',...
     'LineWidth', 1);
%
    axis([0,time(end),axismin,axismax]);

  % Labels
   XaxisLabel = 'Time (seconds)';
   YaxisLabel = 'SPV (degrees/second)';
   XLabel(XaxisLabel, 'FontSize', 8, 'FontWeight', 'bold');
   YLabel(YaxisLabel, 'FontSize', 8, 'FontWeight', 'bold');
 %-------------------------------------------------------------------
 %-------------------------------------------------------------------

end
```

filt_position.m

```
function y = filt_position(x, sample_rate, num_lpf, num_OS, quad_flag)

%
% filt_position - filters the eye position with a Butterworth filter,
%              using 'filtfilt' to remain phase-less
%
% Written by: D. Balkwill 10/20/93
% Modified by: D. Balkwill 8/17/95
%                                          - added "num_lpf" and "num_OS" parameters for
%                                            external control of number of filter stages
%

N1 = sample_rate / 20;
N1 = max(N1, 3);
N1 = min(N1, 10);
N2 = round(1.7 * N1);
N3 = round( (N1 + N2) / 2 );

corner = 28;
[B,A] = butter(2, 2 * corner / sample_rate);   % butterworth filter, fc = 28 Hz

% one stage of OS filtering first, to reduce noise
y = OS_lin2(x, N1, N2);
```

```
%y = OS_lin2(x, 2*N1, 2*N2);          % filters out some of 16 Hz noise

y = filtfilt(B,A,y);
if (num_lpf > 1),
        for i=2:num_lpf,
                y = filtfilt(B,A,y);
        end
end

for i=2:num_OS,
        if (quad_flag),
          y = OS_lin2quad1(y, N1, N2, N3);
        else
          y = OS_lin2(y, N1, N2);   % order statistic filter
        end
end

clear B A N1 N2 N3 I
```

get_patient_list.m

```
function [code_length, patient_list] = get_patient_list(data_path, master_path)

% get_patient_codes - input patient codes for batch processing
%
% D. Balkwill 9/28/93
%

% File modified and converted into a function by Cemocan S. Yesil, Summer
% 2003

check_flag = 1;
code_length = [];
patient_list = [];
[m,n] = size(patient_list);

% Remember the data and master paths if patient_list.mat file exists --
% Cemocan S. Yesil
if (exist([data_path,'patient_list.mat']) == 2),
  eval(['load ',data_path,'patient_list.mat']);
  fprintf('\nCurrent patient list:\n');
  for i=1:length(code_length),
    fprintf([patient_list(i,1:code_length(i)), '\n']);
  end
  yn = get_yn('Is this the correct patient list','Y');
  if (yn == 'Y'),
    check_flag = 0;
  else,
    code_length = [];
    patient_list = [];
  end
end

while (check_flag == 1),

  % terminate list by entering no patient code
  patient_code = input('Enter Subject Code (e.g. aim3s5d1): ','s');
  if (isempty(patient_code) == 1),
    check_flag = 0;
    break;
  end
```

```
   % add run code to patient list, padding with blanks as needed
   l = length(patient_code);
   if (l < n),
      patient_code = [patient_code, zeros(1,n-l)];
   elseif (l > n),
      patient_list = [patient_list, zeros(m,l-n)];
   end
   patient_list = [patient_list; patient_code];
   [m,n] = size(patient_list);
   code_length = [code_length; l];

end

% save the data_path and master_path strings into patient_list.mat to
% automatically use the same path in repetative executions of
% batch_bed_anal and eye_anal_manual -- Cemocan S. Yesil
eval(['save ',data_path,'patient_list.mat patient_list code_length']);
eval(['save ',master_path,'patient_list.mat patient_list code_length']);

return;
```

get_PC_bed_path.m

```
function [master_path, data_path] = get_PC_bed_path

% get_PC_bed_path
%
% This routine searches the MatLab path specification for the main MatLab
%   folder (name ends in MATLAB), and looks in that folder for a file named
%   research_path, which is to contain a string variable named 'data_path'.
%   The contents of 'data_path' is the name of the folder in which the data
%   to be analyzed is stored.
%
% Written by: D. Balkwill  10/20/93
%   Note: same as 'get_rot_path', but with different file name 'research_path'.

% File modified and converted into a function by Cemocan S. Yesil, Summer
% 2003


% see if rotation path exists,input if it doesn't
status = exist(['bed_path.mat']);
if (status == 2),
   eval(['load ', 'bed_path.mat']);

else
   % locate the code files -- Cemocan S. Yesil
   master_path = input('\nEnter matlab file directory (with a backslash at the end): ','s');
   % locate the data files -- Cemocan S. Yesil
   data_path = input('Enter subject data directory (with a backslash at the end): ','s');

end

% % ensure that : is at end of path
% l = length(data_path);
% if (data_path(l) ~= '\'),
%    data_path = [data_path,'\'];
%    status = 1;   % force save with back-slashed path name
% end
%
```

```
% i = length(data_path);
% if (master_path(i) ~= '\'),
%    master_path = [master_path,'\'];
%    status = 1;  % force save with back-slashed path name
% end

% save path if it hasn't been before
if (status ~= 2)
   eval(['save ',master_path,'bed_path.mat master_path data_path']);
end

return;
```

get_yn.m

```
function yn = get_yn( question, default )

%
% yn - asks a yes/no 'question', allowing an answer of 'Y' or 'N'
%      from the user, and returns the capitalized response letter.
%      If the user response is not 'y', 'n', 'Y', or 'N, the response
%      is set to the 'default' value.
%
% Written by: D. Balkwill 9/28/93
%

if ((default >= 'a') & (default <= 'z')),
   default = default - 'a' + 'A';
end

if (default == 'Y'),
   yn = input( [question,' ([Y]/N) ? '],'s');
   other = 'N';
else
   yn = input( [question,' (Y/[N]) ? '],'s');
   other = 'Y';
end

if (isempty(yn)),
   yn = default;
elseif ((yn >= 'a') & (yn <= 'z')),
   yn = yn - 'a' + 'A';
end

if (yn ~= other),
   yn = default;
end

clear other
```

init_bed.m

```
% File modified and converted into a function by Cemocan S. Yesil, 2003
function [FALSE, TRUE, LEFT_VERTICAL, RIGHT_VERTICAL, LEFT_HORIZONTAL, RIGHT_HORIZONTAL,
num_increase, num_RMS, min_diff_class] = init_bed

FALSE = 0;
TRUE = 1;

% Raw data column numbers corresponding to different eyes and axes.
% Corrected by Cemocan S. Yesil on 15 August 2003
```

```
LEFT_VERTICAL = 3;
RIGHT_VERTICAL = 5;
LEFT_HORIZONTAL = 2;
RIGHT_HORIZONTAL = 4;

num_increase = 2;
num_RMS = 0.25;
min_diff_class = 30;

return;
```

interp_blinks.m

```
function spv = interp_blinks(vel, first, last)

% interp_blinks - Interpolates across eye position blinks by calculating new
%           position values to estimate replacement values for blink points.
%           New position values are interpolated as first order line segments.
%           a zeroth order hold.
%
% Written by: D. Balkwill 11/16/93
%
% Modified from "interpolate.m" by: MDB 10/1/99
%
%

spv = vel;
n = length(first);

% replace old velocities with new ones
delta = last - first + 1;
for i=1:n,
   d = delta(i);
          s = vel(first(i));
          e = vel(last(i));
   spv(first(i):last(i)) = (s * ones(d,1)) + ((e - s) * [0:(d-1)]'/(d-1));
end
```

interpolate.m

```
function spv = interpolate(vel, first, last)

% interpolate - Interpolates across fast phases by calculating new SPV
%           values to estimate replacement values for fast phase
%           velocity samples.  New SPV is the median of the three
%           SPV values before the fast phase, and interpolated as
%           a zeroth order hold.
%
% Written by: D. Balkwill 11/16/93
%

spv = vel;
n = length(first);
vn = length(vel);

if (n == 0),
          return;
end

% variables for calculation of new interpolation values
a = first;
```

```
b = last;
m = n;

% eliminate fast phases which are on time boundaries
start_flag = (first(1) == 1);
end_flag = (last(n) == vn);
if (start_flag),        % first phase is at start of time boundary
   a = a(2:m);
   b = b(2:m);
   m = m - 1;
end
if (end_flag),    % last phase is at end of time boundary
   a = a(1:m-1);
   b = b(1:m-1);
   m = m - 1;
end

% check that there are any fast phases left to interpolate across
if (m > 0),

        % construct matrix of velocities before fast phase for speed optimization,
        % and calculate new interpolation values as median of previous three points
        overlap = find(a < 4);
        if (~isempty(overlap)),
                a(overlap) = 4 * ones(size(overlap));
        end
        overlap = find(b > (vn-3));
        if (~isempty(overlap)),
                b(overlap) = (vn-3) * ones(size(overlap));
        end
        vel_matrix = [vel(a-1), vel(a-2), vel(a-3)];
        start_values = median(vel_matrix')';
        vel_matrix = [vel(b+1), vel(b+2), vel(b+3)];
        end_values = median(vel_matrix')';

        % add extrapolation values for fast phases which occurred on time boundaries
        if (start_flag),
           i = last(1) + 1;
           v = median(vel(i:i+2));
           start_values = [v; start_values];
           end_values = [v; end_values];
        end
        if (end_flag),
           i = first(n) - 1;
           v = median(vel(i-2:i));
           start_values = [start_values; v];
           end_values = [end_values; v];
        end

        % replace old velocities with new ones
        delta = last - first + 1;
        for i=1:n,
           d = delta(i);
           s = start_values(i);
           e = end_values(i);
           spv(first(i):last(i)) = (s * ones(d,1)) + ((e - s) * [0:1/(d-1):1]');
        end

end

clear a b m n vn start_flag end_flag overlap vel_matrix start_values end_values i v  delta d s e
```

load_file.m

```
function [run_code, eyeext] = load_file(data_path, patient_list, patnum)

% This loads the appropriate file and eye data for analysis
% Copied from previous eye.m and modified
% By David Phillips, April 1, 2001

% File modified and converted into a function by Cemocan S. Yesil, Summer
% 2003

  file_name = patient_list(patnum,:);
        idx = find(abs(file_name) > 32);                % printable non-blank characters
        file_name = file_name(idx);

        idx = find(file_name == '.');
        if (isempty(idx)),
                root_file = file_name;
        else
                root_file = file_name(1:(idx(1)-1));
        end
  run=input('\nEnter run number: ', 's');

  % assign run extension for .mat filenames -- Cemocan S. Yesil
  rn=str2num(run);
                if (rn < 10),
                        run_code = [root_file, '_run0', run];
                else
                        run_code = [root_file, '_run', run];
                end

  fprintf('\nWhich eye do you want to use for %s?\n', run_code);
  eyenum=input('LV=1, LH=2, RV=3, RH=4 (LV default): ', 's');
  eyenum=str2num(eyenum);

  if isempty(eyenum)
     eyenum=1;
  end

  % Re-structured if loop for eye and axes selection -- Cemocan S. Yesil
  % Assign eye extenstion to .mat filenames -- Cemocan S. Yesil
  if eyenum==1
      eyeext='_LV';
  elseif eyenum==2
      eyeext='_LH';
  elseif eyenum==3
      eyeext='_RV';
  elseif eyenum==4
      eyeext='_RH';
  else
     fprintf('\nInvalid input! Please run eye_anal_manual again.');
  end
```

min_threshold.m

```
function same = min_threshold(x, y, mult, minimum)

% threshold - compare two profiles, and reject all points which differ
%                                 by more than a specified multiple of the rms, and at
%                                 least by 'minimum' units
% Written by: D. Balkwill 10/20/93
```

```
%

d = abs(y - x);
s = sqrt(mean(d .* d));
n = abs(d / s);
same = ((n <= mult) | (d < minimum));
%plot(n)
clear d s n
```

newAATM.m

```
function spv = newAATM(window, vel)

% matAATM - MATLAB implementation of the "newAATM" C-code, since
%                                   the C-code could not be run on the PowerMac as yet.
%
% Written by: MDB 1/18/96
%

% initialize parameter values
ALPHA = 0.44;
BETA = 0.12;
MU = 0.4;

% integer number of samples in sliding window
N = floor(window / 2);
L = round(2 * N + 1);
num_samples = max(size(vel));
stop = num_samples - N;

% initialize skewing parameters
Lalpha = round(L * ALPHA);
Lbeta = round(L * BETA);
M = round(L * MU);

% initialize and sort first window of data
spv = vel;
s = sort(vel(1:L));

% check to see if array is sorted
d = s(2:L) - s(1:(L-1));
j = find(d < 0);
if (~isempty(j)),
        fprintf('Array unsorted initially at indices ');
        j
end

% calculate skewness of first window of data
if (s(L - Lbeta) == s(Lbeta)),
        Sbeta = 0;
else
        Sbeta = (s(L - Lbeta) + s(Lbeta) - 2 * s(N+1));
        Sbeta = Sbeta / (s(L - Lbeta) - s(Lbeta));
end
K = round(- Sbeta * M);

% new value at centre of window is mean of estimated peak of histogram
spv(N+1) = mean( s( (Lalpha + K + 1):(L - Lalpha + K) ) );
%spv(N+1) = mean( s( (Lalpha + K):(L - Lalpha + K - 1) ) );
```

```
% for each value
for n = (N+2):stop,

        old = vel(n - N - 1);% value to be removed from list
        new = vel(n + N);               % value to be inserted into list

        % find index of old value
        k1 = find(s == old);
        if (isempty(k1)),
                disp('ERROR: value not found in vector');
                k1 = 1;
        else
                k1 = k1(1);
        end

if (s(k1) ~= old),
        disp('OLD not found');
end

        %
        % insert new value and remove old value
        %
        if (old == new),      % simple replacement

                s(k1) = new;
                spv(n) = spv(n-1);   % histogram has not changed, so neither has SPV

        else

                % remove old value
                if (k1 == 1),
                        s = s(2:L);
                elseif (k1 == L),
                        s = s(1:(L-1));
                else
                        s = [s(1:(k1-1)); s((k1+1):L)];
                end

                % check for out of bounds of sorted list,
                %       find insertion index for new value,
                %       and insert new value into list
                if (new <= s(1)),
                        k2 = 1;
                        s = [new; s];
                elseif (new >= s(L-1)),
                        k2 = L;
                        s = [s; new];
                else
                        k2 = find(s > new);
                        k2 = k2(1);
                        s = [s(1:(k2-1)); new; s(k2:(L-1))];
                end
%               elseif (new > old),
%                       k2 = find(s((k1+1):L) > new);
%                       k2 = k2(1) + k1 - 1;% new is to the right of old, shift left
%                       s = [s(1:(k1-1)); s((k1+1):k2); new; s(k2+1:L)];
%               else
%                       k2 = find(s(1:k1) > new);
%                       k2 = k2(1);                             % new is to the left of old, shift right
%                       s = [s(1:(k2-1)); new; s(k2:(k1-1)); s(k1+1:L)];
%               end
```

```
% check to see if array is sorted
d = s(2:L) - s(1:(L-1));
j = find(d < 0);
if (~isempty(j)),
        fprintf(['Array unsorted at iteration # ', int2str(n), ' at indices ']);
        j
end

                % calculate skewness of new window of data
                if (s(L - Lbeta) == s(Lbeta)),
                        Sbeta = 0;
                else
                        Sbeta = (s(L - Lbeta) + s(Lbeta) - 2 * s(N+1));
                        Sbeta = Sbeta / (s(L - Lbeta) - s(Lbeta));
                end
                K = round(- Sbeta * M);

                % new value at centre of window is mean of estimated peak of histogram
                spv(n) = mean( s( (Lalpha + K + 1):(L - Lalpha + K) ) );
%               spv(n) = mean( s( (Lalpha + K):(L - Lalpha + K - 1) ) );

        end             %else

end             %for

clear s N L K num_samples stop i k1 k2 new old
clear ALPHA BETA MU Lalpha Lbeta M
```

OS_lin2.m

```
function y = OS_lin2(x,N1,N2)

% This function performs order statistic filtering (first stage
% of Engelken, 1990) on an input signal x to sharpen corners and
% reduce noise.  It uses two windows of length N1 and N2,
% allowing linear root signals.  The new value is therefore
% the median of five values.
%
% D. Balkwill 10/28/90

l = length(x);

% calculate window coefficients for forward filters
h1F = PFMH1(N1);
h2F = PFMH1(N2);

% backward filters have same coefficients, but in reverse
h1B = h1F;
for i=1:N1
   h1B(i) = h1F(N1-i+1);
end
h2B = h2F;
for i=1:N2
   h2B(i) = h2F(N2-i+1);
end

% Use Matlab filter command to maximize speed of execution,
% applying forward and backward windows to appropriate range
% of the input signal.
xF1 = filter(h1F,1,x);
xF1 = [x(1:N1)' xF1(N1:l-1)'];
```

```
xB1 = filter(h1B,1,x);
xB1 = [xB1(N1+1:l)' x(l-N1+1:l)']';

xF2 = filter(h2F,1,x);
xF2 = [x(1:N2)' xF2(N2:l-1)']';
xB2 = filter(h2B,1,x);
xB2 = [xB2(N2+1:l)' x(l-N2+1:l)']';

y = median([x xF1 xB1 xF2 xB2]')';

clear xB1 xF1 xB2 xF2 i l h1F h1B h2F h2B
```

OS_lin2quad2.m

```
function y = OS_lin2quad1(x,N1,N2,N3)

% This function performs order statistic filtering (first stage
% of Engelken, 1990) on an input signal x to sharpen corners and
% reduce noise.  It uses two linear windows of length N1 and N2,
% and ones second-order window of length N3, so that linear and
% parabolic root signals are preserved.  The new value is therefore
% the median of seven values.
%
% D. Balkwill 11/19/93

l = length(x);

% calculate window coefficients for forward filters
h1F = PFMH1(N1);
h2F = PFMH1(N2);
h3F = PFMH2(N3);

% backward filters have same coefficients, but in reverse
h1B = h1F;
for i=1:N1
   h1B(i) = h1F(N1-i+1);
end
h2B = h2F;
for i=1:N2
   h2B(i) = h2F(N2-i+1);
end
h3B = h3F;
for i=1:N3
   h3B(i) = h3F(N3-i+1);
end

% Use Matlab filter command to maximize speed of execution,
% applying forward and backward windows to appropriate range
% of the input signal.
xF1 = filter(h1F,1,x);
xF1 = [x(1:N1)' xF1(N1:l-1)']';
xB1 = filter(h1B,1,x);
xB1 = [xB1(N1+1:l)' x(l-N1+1:l)']';

xF2 = filter(h2F,1,x);
xF2 = [x(1:N2)' xF2(N2:l-1)']';
xB2 = filter(h2B,1,x);
xB2 = [xB2(N2+1:l)' x(l-N2+1:l)']';

xF3 = filter(h3F,1,x);
xF3 = [x(1:N3)' xF3(N3:l-1)']';
```

```
xB3 = filter(h3B,1,x);
xB3 = [xB3(N3+1:l)' x(l-N3+1:l)']';

y = median([x xF1 xB1 xF2 xB2 xF3 xB3]')';

clear xB1 xF1 xB2 xF2 xB3 xF3 i l h1F h1B h2F h2B h3F h3B
```

PFMH1.m

```
function h1 = PFMH1(N)

% This calculates the coefficients for a linear order statistic
% window of length N.
%
% D. Balkwill  10/28/90

a = (4*N + 2)/(N*(N-1));
b = 6/(N*(N-1));
h1 = a * ones(1,N) - b * [1:N];
clear a b ans
```

PFMH2.m

```
function h2 = PFMH2(N)

% This calculates the coefficients for a second-order order statistic
% window of length N.
%
% D. Balkwill  11/19/93

i = [1:N];
h2 = (9 * N * N) + ((9 - 36 * i) * N) + (30 * i .* i) - (18 * i) + 6;
h2 = h2 / (N * (N * N - 3 * N + 2));
%a = (4*N + 2)/(N*(N-1));
%b = 6/(N*(N-1));
%h1 = a * ones(1,N) - b * [1:N];
clear i
```

simple_blinks.m

```
function [blink_start, blink_end] = simple_blinks(pos, num_increase, min_diff_class)
%
% simple_blinks.m  - attempts to detect the blinks in a position trace 'pos'
%
% The ISCAN blink detection algorithm marks "blink" points as zeros.  A blink
%       interval is defined as a series of consecutive blink points.  A specified
%       number of points (num_increase) are added to the beginning and end of the
%       blink interval, to allow for transient behaviour.  In addition, the blink
%       interval is extended to include any consecutive points that differ by more
%       than a specified threshold (min_diff_class).  "blink_start" is a vector in
%       which each element is the sample number of the start of a blink interval.
%       "blink_end" contains the corresponding sample numbers of the ends of the
%       blink intervals.
%
% Suggested values for the input parameters are:
%       pos = raw eye position, uncalibrated
%       num_increase = 2
%       min_diff_class = 100
%
```

```
% Written by: MDB 10/1/99
%

[m,n] = size(pos);
if (m > n),                         % column vector
        last = m;
        d = [0; abs(diff(pos))];
else                                % row vector
        last = n;
        d = [0, abs(diff(pos))];
end

% flag "blink" points
fast = (pos == 0);

% increase fast phase duration by 'num_increase' sample
%   in each direction for transients
if (num_increase > 0),
   fast = filtfilt(ones(num_increase+1,1), 1, fast);
   fast = (fast > 0);
end

% find start and end of each fast phase
fast_diff = filter([1 -1], 1, fast);   % two-point difference
blink_start = find(fast_diff > 0);                  % 0 to 1 transition
num_start = length(blink_start);
blink_end = find(fast_diff < 0) - 1;                        % 1 to 0 transition
num_end = length(blink_end);
if (num_end < num_start),
   blink_end = [blink_end; last];
   num_end = num_end + 1;
end

% extend interval until difference is less than threshold
for i=1:num_end,
        s = blink_start(i);
        while (d(s) > min_diff_class),
                s = s - 1;
        end
        blink_start(i) = s;
        e = blink_end(i);
        while (d(e) > min_diff_class),
    if (e < length(d))
      e = e + 1;  %ERROR here is that d(e) index goes higher than length d. This is index exceeds matrix dimension
    else d(e) = min_diff_class; %If difference too high, make it min threshold
    end
  end
        blink_end(i) = e;
end

return;
```

thresh_blinks.m

```
function [blink_start, blink_end] = thresh_blinks(pos, num_increase, ...
                                                                    low_thresh,
high_thresh, min_diff_class)
%
% thresh_blinks.m  - attempts to detect the blinks in a position trace 'pos'
%
% The ISCAN blink detection algorithm marks "blink" points as zeros.  In some
```

```
%       cases, a blink may be missed by ISCAN, but the value at that point may be
%       above or below a specified non-zero threshold.  A blink interval is
%       defined as a series of consecutive blink points with values < "low_thresh"
%       or > "high_thresh" in addition to the ISCAN zeros.  A specified
%       number of points (num_increase) are added to the beginning and end of the
%       blink interval, to allow for transient behaviour.  In addition, the blink
%       interval is extended to include any consecutive points that differ by more
%       than a specified threshold (min_diff_class). "blink_start" is a vector in
%       which each element is the sample number of the start of a blink interval.
%       "blink_end" contains the corresponding sample numbers of the ends of the
%       blink intervals.
%
% Suggested values for the input parameters are:
%       pos = raw eye position, uncalibrated
%       num_increase = 2
%       min_diff_class = 100
%
% Written by: MDB 10/1/99
%

[m,n] = size(pos);
if (m > n),                     % column vector
        last = m;
        d = [0; abs(diff(pos))];
else                            % row vector
        last = n;
        d = [0, abs(diff(pos))];
end

% flag "blink" points
fast = ((pos <= low_thresh) | (pos >= high_thresh));

% increase fast phase duration by 'num_increase' sample
%   in each direction for transients
if (num_increase > 0),
  fast = filtfilt(ones(num_increase+1,1), 1, fast);
  fast = (fast > 0);
end

% find start and end of each fast phase
fast_diff = filter([1 -1], 1, fast);   % two-point difference
blink_start = find(fast_diff > 0);                      % 0 to 1 transition
num_start = length(blink_start);
blink_end = find(fast_diff < 0) - 1;                            % 1 to 0 transition
num_end = length(blink_end);
if (num_end < num_start),
  blink_end = [blink_end; last];
  num_end = num_end + 1;
end

% extend interval until difference is less than threshold
for i=1:num_end,
        s = blink_start(i);
        while (d(s) > min_diff_class),
                s = s - 1;
        end
        blink_start(i) = s;
        e = blink_end(i);
        while (d(e) > min_diff_class),
                e = e + 1;
        end
        blink_end(i) = e;
```

```
end

return;
```

zero_filter.m

```
function y = zero_filter( B, A, x )

% zero_filter
%
% Performs zero phase shift filtering for FIR filters (ONLY!)
%               by padding signal to be filtered with non-zero values at
%               beginning and end of data sequence.
%    Called with the same parameters and order as Matlab filter command.
%
% Written by: D. Balkwill 10/20/93     (slightly modified from D. Merfeld)
%

% check sizes of vectors
nx=max(size(x));
nB=max(size(B));

% get inital condition for delay
x(nx+1:nx+((nB-1)/2)) = x(nx).*ones(((nB-1)/2),1);
[temp,Zi] = filter( B, A, x(1) .* ones(((nB-1)/2),1) );

% derivative filter with initial condition for phase-shift compensation
x = filter(B,A,x,Zi);
y = x(((nB-1)/2+1):nx+((nB-1)/2));

%clear temp Zi nx nB
```